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## HEPATOTOXIC SUBSTANCES COMMONLY USED AT AIR FORCE BASES

ARMSTRONG

LABORATORY

Elizabeth A. Maull  
Joann M. Jacobsen, Technical Sergeant, USAF

OCCUPATIONAL AND ENVIRONMENTAL HEALTH DIRECTORATE  
Occupational Medicine Division  
2402 E Drive  
Brooks Air Force Base, TX 78235-5114

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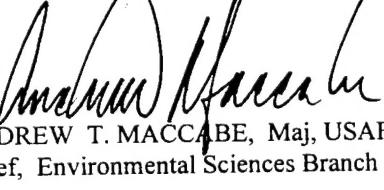
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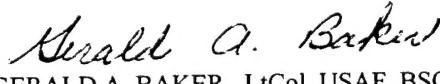
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ANDREW T. MACCABE, Maj, USAF, BSC  
Chief, Environmental Sciences Branch



GERALD A. BAKER, LtCol, USAF, BSC  
Chief, Occupational Medicine Division

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## HEPATOTOXIC SUBSTANCES COMMONLY USED AT AIR FORCE BASES

### Introduction

This Special Report is the result of a request for more information on a list of chemicals commonly used at Air Force facilities and generally considered to be hepatotoxic. There was a concern that some chemicals used by the Air Force might not be included in the commonly used NIOSH Pocket Guide to Chemical Hazards. We have used a variety of databases at our disposal to more thoroughly investigate the potentially hepatotoxic chemicals on the original request list.

### Information Found Within the Report

The report is divided into three sections: 1) the list of hepatotoxic substances commonly used at Air Force bases; 2) occupational exposure values and carcinogenicity classifications for each chemical, (when available); 3) and EPA and ACGIH cancer classification system. The first section contains most of the pertinent toxicological information. Each chemical is given a designation reflecting professional judgment (y or n) and the NIOSH Pocket Guide guidance on hepatotoxicity. NIOSH Target Tissues and critical effects from EPA's Integrated Risk Information System are also included, to provide some information on other physiological systems that may need monitoring. Both the EPA and ACGIH cancer classifications have been included under the heading of HSDB (Hazardous Substances Data Base) Toxic Hazard Rating.

To supplement the information commonly found in the NIOSH and TLV handbooks, we have included information on typical types of medical surveillance and populations at special risk. This information is more for the medical management of the workers exposed to these chemicals. In several cases, information regarding the potential for synergistic interactions were also noted. Often these chemicals are not hepatotoxic in themselves, but may cause problems when mixed exposures occur. The information for these sections was derived almost exclusively from the Hazardous Substances Data Base.

The second section of the Report is a table of regulatory values from ACGIH (TLVs), OSHA (PELs), and NIOSH (RELs). Carcinogenicity classifications have also been included in this section as well as in the first section. The last section is a companion to the first two, as it provides the definitions of the cancer classifications.

### Intent of Report

This report is intended to provide some very specific information to the supervisor on potential hepatotoxicity of a chemical, the appropriate physiological systems to monitor, populations at risk, and other target tissues. It is important to keep in mind the principle "the dose makes the toxin". Just because some of the chemicals have been identified as hepatotoxins does not mean that they will cause a problem whenever there is an exposure to them. In most cases, exposure to small amounts or low concentrations of the chemical will not be a problem. Therefore, identification of a "hepatotoxic" chemical within a product formulation does not necessarily mean that the formulation is of concern. The degree of hazard of the formulation will depend on the specific characteristics of the chemical and the concentration within the formulation and specific exposure routes. Of course, the final call for medical surveillance resides with the Occupational Medicine Physician.

## **HEPATOTOXIC SUBSTANCES COMMONLY USED AT AIR FORCE BASES**

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Acetaldehyde</b>	<b>N</b>

1. IRIS Critical Effects: Degeneration of olfactory epithelium. Short-term Rat Inhalation Studies - Appleman et al., 1986;1982.
2. NIOSH Target Organs: Eyes, skin, respiratory system, kidneys, central nervous system, reproductive system (*in animals; nasal cancer*).
3. HSDB Toxic Hazard Rating: Inadequate evidence of carcinogenicity in humans. Sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans. A3. A3= Animal carcinogen. EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Based on increased incidence of nasal tumors in male and female rats and laryngeal tumors in male and female hamsters after inhalation exposure. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient.
4. HSDB Population at Special Risk: Workers with chronic respiratory, liver, kidney, or skin diseases.

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<b>Substance</b>	<b>Hepatotoxic</b>
<b>Acetic Acid</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, teeth.
2. HSDB Medical Surveillance: Employment and periodic medical exam should be carried out to ensure that workers with respiratory ailments, skin disorders or keratoconjunctivitis are protected from exposure to acetic acid.
3. HSDB Populations at Special Risk: Employees with chronic respiratory, skin, or eye disease are at increased risk from acetic acid exposure.

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<b>Substance</b>	<b>Hepatotoxic</b>
<b>Acetone</b>	<b>N</b>

1. IRIS Critical Effects: Increase liver and kidney weights and nephrotoxicity. Rat Oral Subchronic Study - U.S. EPA, 1986.
2. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: Based on lack of data concerning carcinogenicity in humans or animals. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.
4. HSDB Medical Surveillance: Urinary glucaric acid and the ratio between 6-beta-OH-cortisol and 17-OH-corticosteroids were determined in chemical workers exposed to styrene greater than or equal to 164 mg/cu m, and acetone greater than or equal to 571 mg/cu m, and in a control group. Exposed workers had significantly higher excretion of glucaric acid and a higher ratio. Urinary mercapturic acids were also increased. Simultaneous styrene and acetone exposure induces mono-oxygenases in humans.
5. Under unusual conditions, potentiation may occur. In animal experiments inhalation and oral administration of acetone both potentiated carbon tetrachloride toxicity.

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

Substance	Hepatotoxic
<b>Acetonitrile*</b>	<b>Y</b>

1. NIOSH Target Organs: Respiratory system, cardiovascular system, liver, kidneys.
2. HSDB Medical Surveillance: Determination of blood cyanide or urinary thiocyanate should not be relied on as evidence for brief inhalation of lower concern of vapor. In biological monitoring, pre-exposure levels should be established, since smokers show elevated concern of metabolites. Consider the skin, resp tract, heart, CNS, renal and liver function in placement and periodic exam.
3. HSDB Populations at Special Risk: Protect from exposure those individuals with diseases of central nervous system, heart and lung.

Substance	Hepatotoxic
<b>Acrolein</b>	<b>N</b>

1. IRIS Critical Effects: Squamous metaplasia and neutrophilic infiltration of nasal epithelium. Subchronic Rat Inhalation Studies - Kutzman, 1981; Feron et al., 1978.
2. NIOSH Target Organs: Eyes, skin, respiratory system, heart.
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: C; possible human carcinogen. Basis for classification: Classification is based on increased incidence of adrenal cortical adenomas to female rats and carcinogenic potential of an acrolein metabolite. Acrolein is mutagenic in bacteria and is structurally related to probable or known human carcinogens. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Limited.
4. HSDB Medical Surveillance: Initial Medical Examination: A complete medical history and physical examination with emphasis on the heart and lungs: The purpose is to detect existing medical conditions which might place the exposed employee at increased risk from reported effects of acrolein, and to establish a baseline for future health monitoring. Examination of the heart and lungs should be stressed. 14"x17" chest roentgenogram: Acrolein may cause lung damage. Surveillance of the lungs is indicated. Forced Vital Capacity and Forced Expiratory Volume (1 sec): Acrolein is reported to cause decreased pulmonary function. Periodic surveillance is indicated. Periodic Medical Examinations: The aforementioned medical examination should be repeated on an annual basis, except that an x-ray is considered necessary only when indicated by the results of the pulmonary function tests.
5. HSDB Populations at Special Risk: Since acrolein is a component of tobacco and marijuana smoke, people exposed to these smokes are a group at increased risk from inhaled acrolein. In addition, acrolein is generated by the thermal decomposition of fat, so cooks are probably also at additional risk. Since acrolein has been shown to suppress pulmonary antibacterial defenses, individuals with or prone to pulmonary infections may also be at a greater risk from exposure to this compound.

Substance	Hepatotoxic
<b>Acrylamide</b>	<b>N</b>

1. IRIS Critical Effects: Nerve damage. Rat Subchronic Drinking Water Study - Burek et al., 1980.
2. NIOSH Target Organs: Eyes, skin, central nervous system, peripheral nervous system, reproductive system (*in animals; tumors of the lungs, testes, thyroid and adrenal glands*).
3. HSDB Toxic Hazard Rating: Evaluation: There is inadequate evidence in humans for the carcinogenicity of acrylamide. There is sufficient evidence in experimental animals for the

carcinogenicity of acrylamide. In making the overall evaluation, the Working Group took into consideration the following supporting evidence: (1) Acrylamide and its metabolite glycidamide form covalent adducts with DNA in mice and rats. (2) Acrylamide and glycidamide form covalent adducts with hemoglobin in exposed humans and rats. (3) Acrylamide induces gene mutations and chromosomal aberrations in germ cells of mice and chromosomal aberrations in germ cells of rats and forms covalent adducts with protamines in germ cells of mice *in vivo*. (4) Acrylamide induces chromosomal aberrations in somatic cells of rodents *in vivo*. (5) Acrylamide induces gene mutations and chromosomal aberrations in cultured cells *in vitro*. (6) Acrylamide induces cell transformation in mouse cell lines. Overall evaluation: Acrylamide is probably carcinogenic to humans, Group A2.

4. HSDB Medical Surveillance: Annual exam with special attention to central nervous system. Preclude from exposure those individuals with diseases of central nervous system. Recommended medical surveillance: The following medical procedures should be made available to each employee who is exposed to acrylamide at potentially hazardous levels: Initial Medical Examination: A complete history and physical examination: The purpose is to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the skin, eyes, and central and peripheral nervous systems should be stressed. The skin should be examined for evidence of chronic disorders. Periodic Medical Examination: The aforementioned medical examinations should be repeated on an annual basis. Emphasis should be placed on informing the employee to report any symptoms associated with acrylamide toxicity. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.

5. HSDB Populations at Special Risk: Protect from exposure individuals with diseases of the central nervous system. Individuals with diseases of the skin, eyes, and peripheral nervous system may be at an increased risk from exposure to acrylamide.

Substance	Hepatotoxic
Acrylonitrile*	Y

1. NIOSH Target Organs: Eyes, skin, cardiovascular system, **liver**, kidneys, central nervous system (*brain tumors, lung and bowel cancer*).
2. HSDB Toxic Hazard Rating: CLASSIFICATION: B1; probable human carcinogen. Basis for Classification: The observation of a statistically significant increase in the incidence of lung cancer in exposed workers and observation of tumors, generally astrocytomas in the brain, in studies in two rat strains exposed by various routes (drinking water, gavage, and inhalation) forms the basis for this classification. [U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Acrylonitrile (107-13-1) from the National Library of Medicine's TOXNET System, March 28, 1994.]
3. HSDB Populations at Special Risk: Protect from exposure those individuals with pulmonary and **liver** diseases.

Substance	Hepatotoxic
Aldrin*	Y

1. IRIS Critical Effects: **Liver toxicity**. Rat Chronic Feeding Study - Fitzhough et al., 1964.
2. NIOSH Target Organs: Cancer, central nervous system, **liver**, kidneys, skin (*in animals, tumors of the lungs, liver, thyroid and adrenal glands*).

3. HSDB Toxic Hazard Rating: Inadequate evidence of carcinogenicity in humans. Limited evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans. EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Orally administered aldrin produced significant increases in tumor responses in three different strains of mice in both males and females. Tumor induction has been observed for structurally related chemicals, including dieldrin, a metabolite. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient.

4. HSDB Medical Surveillance: Initial Medical Examination: A complete history and physical examination: The purpose is to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the nervous system and liver should be stressed. The aforementioned medical examination should be repeated on an annual basis. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.

5. HSDB Populations at Special Risk: Individuals with liver disease. Individuals who have a history of convulsive disorders maybe at an increased risk.

Substance	Hepatotoxic N
<b>Ammonia</b>	

1. NIOSH Target Organs: Eyes, skin, respiratory system.

2. HSDB Toxic Hazard Rating: Ammonia in an aqueous environment exists in equilibrium between ionized ammonium action and the non-ionized ammonia. This equilibrium can be affected by buffers, pH, temperature, and salinity. Thus in many cases it is not possible to assign the associated toxicity to the ionized or non-ionized form of the ammonia-nitrogen.

3. HSDB Medical Surveillance: The following medical procedures should be made available to each employee who is exposed to ammonia at potentially hazardous levels: (1) A complete medical history and physical examination: The purpose is to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the eyes and respiratory tract should be stressed. The skin should be examined for evidence of chronic disorders; (2) 14" x 17" chest roentgenogram: Ammonia causes human lung damage. Surveillance of the lungs is indicated; (3) FVC and FEV (1 sec): Ammonia is a respiratory irritant. Persons with impaired pulmonary function may be at increased risk from exposure. Periodic surveillance is indicated. Medical examinations should be repeated on an annual basis, except that an X-ray is necessary only when indicated by the results of pulmonary function testing, or by signs and symptoms of respiratory disease.

4. HSDB Populations at Special Risk: In the event an individual's liver function is greatly reduced, any source of ammonia, such as inhalation, can lead to hepatic coma with increased circulating ammonia. Persons with corneal disease, and glaucoma, or chronic respiratory diseases may suffer increased risk.

Substance	Hepatotoxic N
<b>n-Amyl Acetate</b>	

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.

Substance	Hepatotoxic N
<b>Antimony and Compounds</b>	

1. NIOSH Target Organs: Eyes, skin, respiratory system, cardiovascular system.

2. HSDB Medical Surveillance: Periodic chest X-ray, pulmonary function testing, and electrocardiogram required.

Substance	Hepatotoxic
<b>Aroclor 1242 and 1254 (PCB's)*</b>	<b>Y</b>

1. IRIS Critical Effects: Ocular exudate, inflamed and prominent Meibomian glands, distorted growth on finger and toe nails; decreased antibody (IgG and IgM) response to sheep erythrocytes. Monkey Clinical and Immunologic Studies - Arnold et al., 1994a,b - Tryphonas et al., 1989, 1991a,b.
2. NIOSH Target Organs: Skin, eyes, reproduction system (*in animals; tumors of the pituitary gland, liver, leukemia*).
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: **Hepatocellular carcinomas** in three strains of rats and two strains of mice and inadequate yet suggestive evidence of excess risk of **liver** cancer in humans by ingestion and inhalation or dermal contact. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient.
4. HSDB Medical Surveillance: Medical records should be kept for the entire length of employment of each worker and for the following 30 yr. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.

Substance	Hepatotoxic
<b>Benzene</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, blood, central nervous system, bone marrow (*leukemia*).
2. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) evidence in humans: sufficient; 2) evidence in animals: sufficient; Overall summary evaluation of carcinogenic risk to humans is group 1: The chemical is carcinogenic to humans. EPA CLASSIFICATION: A; human carcinogen. Basis for Classification: Several studies of increased incidence of nonlymphocytic leukemia from occupational exposure, increased incidence of neoplasia in rats and mice exposed by inhalation and gavage, and some supporting data form the basis for this classification. Notice of Intended Changes (1993-94): These substances, with their corresponding values, comprise those for which either a limit has been proposed for the first time, for which a change in the "Adopted" listing has been proposed, or for which retention on the Notice of Intended Changes has been proposed. In all cases, the proposed limits should be considered trial limits that will remain in the listing for a period of at least one year. If, after one year no evidence comes to light that questions the appropriateness of the values herein, the values will be reconsidered for the "Adopted" list. A1. A1= Confirmed Human Carcinogen.
3. HSDB Medical Surveillance: If individuals are known to be exposed to benzene vapors in their working environment prophylactic measures should be taken. All possible methods should be used to protect such persons against breathing the fumes. They should have periodic physical exam, including blood studies. In addition the urine should be examined at intervals to determine extent of excretion of conjugation products. Once poisoning has developed it is essential to prevent further exposure. Assessment of fitness should include consideration of previous medical & occupational history. Occupational history should take into account any previous exposure to benzene, radiomimetic substances or ionizing radiation. Medical exam should include thorough physical & hematological examination. The latter should cover hemoglobin determination, red cell, white cell & platelet counts, white cell differential count & red cell & leukocyte morphology. Protect young persons of either sex under 18 yr of

age from exposure to benzene since adolescents have lower resistance to bone-marrow poisons. Pregnant women & nursing mothers should not be exposed & special precautions are necessary where women of childbearing age are exposed to benzene hazard. Subjects with liver diseases & microcytopenia should not be exposed. Periodic exam should be carried out in same way as pre-employment examination. Particular attention should be paid to any hematological abnormalities found during 1st periodic examination. Whenever there is slightest suspicion of leukemia, a bone-marrow biopsy is warranted. Biological monitoring: The current required regular physical exam should include blood pressure check, lung functions, blood chemistry, hematology, urinalysis & skin exam. PRECAUTIONS FOR "CARCINOGENS": In relation specifically to cancer hazards, there are at present no health monitoring methods that may ensure the early detection of preneoplastic lesions or lesions which may preclude them. Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning additional tests that might become useful or mandatory.

4. HSDB Populations at Special Risk: Individuals with G6PD glucose 6-Phosphate dehydrogenase deficiency have been found to be more susceptible to hemolytic effects of benzene. It has been observed that levels of leukocyte agglutins were elevated in selected individuals exposed to benzene. This suggested that in some people benzene toxicity may be accounted for in part by an allergic blood dyscrasia.

Substance	Hepatotoxic
<b>Benzoyl Peroxide</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system.

Substance	Hepatotoxic
<b>Beryllium and compounds</b>	N

1. IRIS Critical Effects: No adverse effects in drinking water. Rat Chronic Oral Bioassay - Schoreder and Mitchner, 1975.

2. NIOSH Target Organs: Eyes, skin, respiratory system (*lung cancer*).

3. HSDB Toxic Hazard Rating: Evaluation: There is sufficient evidence in humans for the carcinogenicity of beryllium and beryllium compounds. There is sufficient evidence in experimental animals for the carcinogenicity of beryllium and beryllium compounds. Overall evaluation: Beryllium and beryllium compounds are carcinogenic to humans (Group 1). EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Beryllium has been shown to induce lung cancer via inhalation in rats and monkeys and to induce osteosarcomas in rabbits via intravenous or intramedullary injection. Human epidemiology studies are considered to be inadequate. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient. A2. A2= Suspected human carcinogen.

4. HSDB Medical Surveillance: In a study of occupational liver diseases, it was noted that beryllium workers frequently experience granulomatous hepatitis which can be confirmed by a positive patch test with beryllium fluoride or sulfate, or confirming the presence of beryllium in the tissues or urine.

PRECAUTIONS FOR "CARCINOGENS": In relation specifically to cancer hazards, there are at present no health monitoring methods that may ensure the early detection of preneoplastic lesions or lesions which may preclude them. Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning additional tests that might become useful or mandatory. Protect from exposure those individuals with previous pulmonary diseases; vital capacity depression of 10% or more; chronic conditions of skin, liver, kidney, heart; and abnormal chest x-rays or blood counts. Special attention to all exposed employees with unexplained or prolonged respiratory symptoms. Protect from further exposure those individuals that become sensitized. It is

recommended that employees in refinery, alloy or ceramic processes should have ventilator function tests performed.

Substance	Hepatotoxic
<b>1,3-Butadiene</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, respiratory system, central nervous system, reproductive system (*hematopoietic cancer*).
2. HSDB Toxic Hazard Rating: Evaluation: There is limited evidence for the carcinogenicity in humans of 1,3-butadiene. There is sufficient evidence for the carcinogenicity in experimental animals of 1,3-butadiene. Studies in vitro suggest that the metabolism of 1,3-butadiene is qualitatively similar in humans and experimental animals. 1,3-Butadiene is metabolized in mammals to epoxy metabolites which interact with DNA. Base-substitution mutations are induced in bacteria. Similar mutations in the K-ras oncogene have been reported in tumors induced in mice by 1,3-butadiene. Overall evaluation: 1,3-Butadiene is probably carcinogenic to humans (Group 2A). EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Inadequate human data and sufficient rodent (mouse and rat) studies in which exposure to airborne concentrations of 1,3-butadiene caused multiple tumors and tumor types form the basis for this classification. Related compounds are carcinogenic and mutagenic. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient. A2. A2= Suspected human carcinogen.
3. HSDB Medical Surveillance: Routine medical examinations should be provided to each employee who is exposed to butadiene at potentially hazardous levels. Health effects to consider Cancer; teratogenicity; reproductive effects. Appropriate engineering ad work-practice controls.

Substance	Hepatotoxic
<b>2-Butanone (MEK)</b>	<b>N</b>

1. IRIS Critical Effects: Decreased fetal birth weight. Multigeneration/Developmental Rat Feeding Study, Cox et al., 1975; Mouse Developmental Study, Schwetz et al., 1991; Mast et al., 1989.
2. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: Based on no human carcinogenicity data and inadequate animal data. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.
4. HSDB Medical Surveillance: Annual physical examinations which include blood cell counts. Protect from exposure individuals with diseases of the skin, blood and central nervous system.

Substance	Hepatotoxic
<b>2-Butoxyethanol*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, hematopoietic system, blood, kidneys, liver, lymphoid system.
2. HSDB Medical Surveillance: Consider the points of attack (liver, kidneys, lymphoid system, skin, blood, eyes, respiratory system) in placement and periodic physical examinations.

Substance	Hepatotoxic
<b>n-Butyl acetate</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
2. HSDB Medical Surveillance: Consider initial effects on skin and resp tract in any placement or periodical exam, as well as liver and kidney function.
3. HSDB Populations at Special Risk: Employees with skin disease, kidney disease, chronic respiratory disease, and liver disease may be at increased risk from butyl acetate exposure.

Substance	Hepatotoxic
<b>sec-Butyl Acetate</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
2. HSDB Medical Surveillance: Consider initial effects on skin and resp tract in any placement or periodical exam, as well as liver and kidney function.
3. HSDB Population at Special Risk: Employees with skin, kidney, chronic respiratory, or liver disease may be at increased risk from sec-butyl acetate exposure.

Substance	Hepatotoxic
<b>tert-Butyl Acetate</b>	N

1. NIOSH Target Organs: Respiratory system, skin, central nervous system.
2. HSDB Medical Surveillance: Consider initial effects on skin and resp tract in any preplacement or periodical exam, as well as liver, and kidney function.
3. HSDB Population at Special Risk: Employees with kidney, chronic respiratory, liver, or skin disease may be at increased risk from tert-butyl acetate exposure.

Substance	Hepatotoxic
<b>Butyl Mercaptan*</b>	Y

1. NIOSH Target Organs: Eyes, skin, respiratory system, liver, kidneys.
2. HSDB Medical Surveillance: Prior to placing a worker in a job with a potential for exposure to n-butyl mercaptan, the physician should evaluate and document the worker's baseline health status with thorough medical, environmental, and occupational histories, a physical examination, and physiologic and laboratory tests appropriate for the anticipated occupational risk. These should concentrate on the function and integrity of the nervous and respiratory systems. Medical surveillance for respiratory disease should be conducted by using the principles and methods recommended by NIOSH and the American Thoracic Society (ATS). A preplacement medical evaluation is recommended in order to detect and assess preexisting or concurrent conditions which may be aggravated or result in increased risk when a worker is exposed to n-butyl mercaptan at or below the NIOSH REL. The examining physician should consider the probable frequency, intensity, and duration of exposure, as well as the nature and degree of the condition, in placing such a worker. Such conditions, which should not be regarded as absolute contraindications to job placement, include chronic diseases of the respiratory system.

Substance	Hepatotoxic
Cadmium (as Cd)	N

1. IRIS Critical Effects: Significant proteinuria (water). Human Studies involving chronic exposures (food) - U.S. EPA, 1985.
2. NIOSH Target Organs: Respiratory system, kidneys, prostate, blood (*prostatic and lung cancer*).
3. HSDB Toxic Hazard Rating: Evaluation: There is sufficient evidence in humans for the carcinogenicity of cadmium and cadmium compounds. There is sufficient evidence in experimental animals for the carcinogenicity of cadmium compounds. There is limited evidence in experimental animals for the carcinogenicity of cadmium metal. In making the overall evaluation, the Working Group took into consideration the evidence that ionic cadmium causes genotoxic effects in a variety of types of eukaryotic cells, including human cells. Overall evaluation: Cadmium and cadmium compounds are carcinogenic to humans (Group 1). A2. A2= Suspected human carcinogen. Cadmium, elemental and compound, as Cd; Total dust; Respirable fraction. EPA CLASSIFICATION: B1; probable human carcinogen. Basis for Classification: Limited evidence from occupational epidemiologic studies of cadmium is consistent across investigators and study populations. There is sufficient evidence of carcinogenicity in rats and mice by inhalation and intramuscular and subcutaneous injection. Seven studies in rats and mice wherein cadmium salts (acetate, sulfate, chloride) were administered orally have shown no evidence of carcinogenic response. HUMAN CARCINOGENICITY DATA: Limited.
4. HSDB Medical Surveillance: Urinary excretion of cadmium is partly correlated to relatively recent exposure. Concern of cadmium in blood is a more direct indicator of exposure than is urinary cadmium. Initial medical examination: a complete history and physical examination detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the respiratory system, liver, kidneys, prostate, and blood should be stressed. Since kidney damage has been observed in humans exposed to cadmium, a urinalysis should be obtained to include, at minimum: specific gravity, albumin, glucose, and a microscopic examination of the centrifuged sediment. In addition, the urine should be examined for low molecular weight proteins by use of 3% sulfosalicylic acid or other acceptable techniques. A 14 x 17 in roentgenogram should be obtained as cadmium causes human lung damage. Surveillance of the lungs is recommended. A profile of liver function should be obtained by utilizing a medically acceptable array of biochemical tests, since cadmium may cause liver damage. FVC and FEV (1 sec): cadmium is reported to cause decreased pulmonary function. Therefore periodic surveillance is recommended. Medical examinations should be repeated annually, except that X-ray is considered necessary only when indicated by pulmonary function tests or by symptoms of respiratory disease. Urine protein measurements should be available every four months.
5. HSDB Populations at Special Risk: Populations at special risk include individuals with: Renal disease of other etiology, which may add to or magnify the effect of cadmium on the kidney; genetic differences in the induction of metallothionein in response to cadmium exposure; dietary deficiencies in metal ions and or protein, which may increase cadmium absorption from the gastrointestinal tract; and, neonates or young children possibly having higher gastrointestinal absorption rates than adults. Occupational exposure: Exposure occurs primarily in smelting and refining zinc, lead and copper ores containing cadmium, spraying cadmium-containing pigments, processing scrap containing cadmium, etc., cadmium alloys, compounds.

Substance	Hepatotoxic
Carbaryl (Sevin, pesticide)	N

1. IRIS Critical Effects: Kidney and liver toxicity. Rat Chronic Feeding Study - Carpenter et al., 1961.

2. NIOSH Target Organs: Respiratory system, central nervous system, cardiovascular system, skin, blood cholinesterase, reproductive system.

3. HSDB Medical Surveillance: Initial Medical Examination: A complete history and physical examination: The purpose is to detect pre existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the respiratory system, cardiovascular system, and central nervous system should be stressed. The skin should be examined for evidence of chronic disorders. Urinalysis: Carbaryl may cause kidney damage. A urinalysis should be performed to include, at a minimum, specific gravity, albumin, glucose, and a microscopic examination of centrifuged sediment. Medical warning: Exposure should be minimized during pregnancy. Periodic Medical Examination: The aforementioned medical examinations should be repeated on an annual basis.

Substance	Hepatotoxic Y
<b>Carbon Disulfide*</b>	

1. IRIS Critical Effects: Fetal toxicity/malformations. Rabbit Inhalation Teratogenic Study - Hardin et al., 1981.

2. NIOSH Target Organs: Central nervous system, peripheral nervous system, cardiovascular system, eyes, kidneys, liver, skin, reproduction system.

3. HSDB Medical Surveillance: A complete history and physical examination: The purpose is to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the central and peripheral nervous systems, eyes, cardiovascular system, kidneys, and liver should be stressed. The skin should be examined for evidence of chronic disorder. Since kidney damage has been observed in humans exposed to carbon disulfide, a urinalysis should be obtained to determine, at a minimum, specific gravity, albumin and glucose content, along with a microscopic examination of centrifuged sediment. Since liver damage has been observed in humans exposed to carbon disulfide, a profile of liver function should be obtained by using a medically acceptable array of biochemical tests. An electrocardiogram: carbon disulfide has caused arrhythmias and electrocardiographic changes in humans. Periodic surveillance is indicated. Carbon disulfide has caused ocular changes in humans. An ophthalmic examination should be performed, including visual acuity. Workers should be informed of potential undesirable effects of exposure to carbon disulfide on reproduction (such as spermatic deficiencies, menstrual disorders, and spontaneous abortions).

4. HSDB Populations at Special Risk: Employees at increased risk: those with problems concerning central and peripheral nervous systems, eyes, cardiovascular system, kidneys, and liver, & SRP: alcoholics.

Substance	Hepatotoxic Y
<b>Carbon Tetrachloride*</b>	

1. IRIS Critical Effects: Liver lesions. Subchronic Rat Gavage Study, Bruckner et al., 1986.

2. NIOSH Target Organs: Central nervous system, lungs, liver, kidneys, skin (*in animals; liver cancer*).

3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Carcinogenicity in rats, mice, and hamsters. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient. Inadequate evidence of carcinogenicity in humans. Sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans. A3, skin. A3= Animal carcinogen.

4. HSDB Medical Surveillance: A complete history and physical examination to detect preexisting conditions and to establish a baseline for future health monitoring. Examination of the **liver** and kidneys, along with examination of the skin and eyes for evidence of chronic disorders. Urinalysis should include at a minimum specific gravity, albumin, glucose, and microscopic examination of centrifuged sediment. These medical examinations should be repeated on an annual basis. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.

5. HSDB Populations at Special Risk: Individuals who are habitual users of barbiturates. The unborn. Individuals at risk include those with conditions of the **liver** and kidneys. Protect from exposure individuals with a history of alcoholism or central nervous system disorders. Very obese or undernourished persons suffering from pulmonary diseases, gastric ulcers, **liver** or kidney diseases, diabetes or glandular disturbances seem especially sensitive to the toxic effects of carbon tetrachloride.

Substance	Hepatotoxic
<b>Chlorobromomethane (Halon 1011)*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, **liver**, kidneys, central nervous system.

2 HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: Based on the lack of data regarding the carcinogenicity of bromochloromethane in humans or animals; however, there are data indicative of genotoxic effects and structural relationships to halogenated methanes classified as B2 probable human carcinogens. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.

3. HSDB Medical Surveillance: Consider the points of attack skin, **liver**, kidneys, respiratory system, lungs, CNS in preplacement and periodic physical exam. The following medical procedures should be made available to each employee who is exposed to chlorobromomethane at potentially hazardous levels: Initial Medical Screening: Employees should be screened for history of certain medical conditions (listed below) which might place the employee at increased risk from chlorobromomethane. Skin disease: Chlorobromomethane can cause dermatitis on prolonged exposure. Persons with existing skin disorders may be more susceptible to effects of this agent. Liver disease: **Although chlorobromomethane is not known as a liver toxin in humans, the importance of this organ in the biotransformation and detoxification of foreign substances should be considered before exposing persons with impaired liver function.** Kidney disease: Although chlorobromomethane is not known as a kidney toxin in humans, the importance of this organ in the elimination of toxic substances justifies special consideration in those with impaired renal function. Chronic respiratory disease: In persons with impaired pulmonary function, especially those with obstructive airway disease, the breathing of chlorobromomethane might cause exacerbation of symptoms due to its irritant properties. 2. Periodic medical exam: Any employee developing the above listed conditions should be referred for further medical examination.

4. HSDB Populations at Special Risk: Persons with existing skin disorders may be more susceptible to the effects of this agent. In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of chlorobromomethane might cause exacerbation of symptoms due to its irritant properties.

Substance	Hepatotoxic
<b>Chloroform*</b>	<b>Y</b>

1. IRIS Critical Effects: Fatty cyst formation on **liver**. Bioassay - Heywood et al., 1979.

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

2. NIOSH Target Organs: Liver, kidneys, heart, eyes, skin, central nervous system (*in animals; liver and kidney cancer*).

3. HSDB Toxic Hazard Ratings: EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Based on increased incidence of several tumor types in rats and three strains of mice. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient. Inadequate evidence of carcinogenicity in humans. Sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans. A2. A2= Suspected human carcinogen.

4. HSDB Medical Surveillance: Initial Medical Examination: A complete history and physical examination to detect preexisting conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of liver, kidneys, and heart should be stressed. The skin should be examined for evidence of chronic disorders. A profile of liver function should be obtained by using a medically acceptable array of biochemical tests. Since kidney damage has also been observed from exposure to chloroform, a urinalysis should be obtained to include at a minimum: specific gravity, albumin, glucose, and a microscopic examination of centrifuged sediment. Periodic Medical Examination: The aforementioned medical examinations should be repeated on an annual basis. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.

5. HSDB Populations at Special Risk: Individuals with diseases of liver, kidneys, or CNS. A history of, or physical signs consistent with, chronic alcoholism probably constitutes an increased risk for employees exposed to chloroform.

Substance	Hepatotoxic
<b>Chromic Acid and Chromate's (as CrO<sub>3</sub>)*</b>	<b>Y</b>

1. NIOSH Target Organs: Blood respiratory system, liver, kidneys, eyes, skin (*lung cancer*).

2. HSDB Toxic Hazard Ratings: Classification of carcinogenicity: 1) evidence in humans: Sufficient; 2) evidence in animals: sufficient. Overall summary evaluation of carcinogenic risk to humans is Group 1: The agent is carcinogenic to humans. Hexavalent chromium compounds EPA CLASSIFICATION: A; The agent is carcinogenic to humans. Basis for Classification: Results of occupational epidemiologic studies of chromium-exposed workers are consistent across investigators and study populations. Dose-response relationships have been established for chromium exposure and lung cancer. Chromium-exposed workers are exposed to both chromium III and chromium VI compounds. Because only chromium VI has been found to be carcinogenic in animal studies, however, it was concluded that only chromium VI be classified as a human carcinogen. HUMAN CARCINOGENICITY DATA: Sufficient.

3. HSDB Medical Surveillance: PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.

Substance	Hepatotoxic
<b>Chromium Metal (as Cr)</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system.

2. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) Evidence in humans: Inadequate; 2) evidence in animals: Inadequate. Overall summary evaluation of carcinogenic risk to humans is group 3: The chemical is not classifiable as to its carcinogenicity to humans. From table, trivalent chromium

compound. Notice of Intended Change (first notice appeared in 1993-94 edition): The ACGIH has listed chemicals for which it has been proposed to delete their "adopted" Short Term Exposure Limits. The proposed deletion should be considered trial proposal that will remain in the listing for a period of at least two years. If, after two years no evidence comes to light that questions the appropriateness of the deletion, it will be reconsidered to remove the values from the "adopted" list. A4. A4= Not Classifiable as a Human Carcinogen.

4. HSDB Medical Surveillance: Residual scars in individuals afflicted with ulcers on the hands, arms, and feet serve as a criterion to physicians in the diagnosis of chromium sensitivity. Reporting Signs and Symptoms: A physician should be contacted if anyone develops any signs or symptoms and suspects that they are caused by exposure to chromium metal or insoluble chromium salts. Chromium metal or insoluble chromium salts. Initial Medical Examination: a) A complete history and physical examination: The purpose is to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the respiratory system should be stressed. b) 14" x 17" chest roentgenogram: Chromium and its insoluble salts may cause human lung damage. Surveillance of the lung is indicated. c) FVC and FEV (1 sec): Insoluble chromium salts are reported to cause decreased pulmonary function. Periodic surveillance is indicated. 2) Periodic Medical Examination: The aforementioned medical examinations should be repeated on an annual basis. Chromium metal or insoluble chromium salts. Preemployment physical exam should include: a work history to determine past exposure to chromic acid and hexavalent Cr compound, exposure to other carcinogens, smoking history, history of skin or pulmonary sensitization to Cr, history or presence of dermatitis, skin ulcers, or lesions of the nasal mucosa and/or perforation of the septum, and a chest x-ray. On periodic exam an evaluation should be made of skin and respiratory complaints, especially in workers who demonstrate allergic reactions. Chest x-ray should be taken yearly for workers over 40, and every five years for younger workers. Blood, liver, and kidney function should be evaluated periodically.

5. HSDB Populations at Special Risk: The effects of chromium compounds on the skin are caused primarily by direct contact. Most of the effects have occurred in occupational settings, and as expected, with more men than women reporting these effects. Chromium compounds. There is sufficient evidence for increased incidence of lung cancer among workers in the chromate producing industry and possibly also among chromium platers and chromium alloy workers.

Substance	Hepatotoxic
<b>Coal Tar Pitch Volatiles</b>	N

1. NIOSH Target Organs: Respiratory system, skin, bladder, kidneys (*lung, kidney and skin cancer*).

Substance	Hepatotoxic
<b>Cobalt Dust and Fume</b>	N

1. NIOSH Target Organs: Skin, respiratory system.
2. HSDB Toxic Hazard Rating: A3. A3= Animal carcinogen. Cobalt, elemental, and inorganic compound, as Co.
3. HSDB Medical Surveillance: The following medical procedures should be made available to each employee who is exposed to cobalt metal fumes and dust at potentially hazardous levels. Initial medical examination: A complete history and physical examination: The purpose is to detect conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the respiratory system should be stressed. The skin should be examined for evidence of chronic disorders. 14x17 inch chest roentgenogram: Cobalt may cause human lung damage. Surveillance of the lungs is indicated. Forced Vital Capacity and Forced Expiatory Volume (1 sec): Cobalt is reported to decrease pulmonary function. Periodic surveillance is indicated. Periodic medical

examination: The aforementioned medical examinations should be repeated on an annual basis. In preemployment exam, special attention should be given to a history of skin diseases, allergic dermatitis, baseline allergic resp diseases, and smoking history. Periodic exam should be directed toward skin and respiratory symptoms and lung function.

4. HSDB Populations at Special Risk: Protect from exposure those individuals with diseases of skin and lung. Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. Contaminated clothing should not be taken home at end of shift, but should remain at employee's place of work for cleaning. Workers with history of skin diseases performing jobs where skin contact occurs.

Substance	Hepatotoxic
<b>Copper Dust and Mist*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, liver, kidneys (*increased risk with Wilson's disease*).
2. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: There are no human data, inadequate animal data from assays of copper compounds, and equivocal mutagenicity data. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.
3. HSDB Medical Surveillance: Consider the skin, eyes, and respiratory system in any placement or periodic examinations.
4. HSDB Populations at Special Risk: Persons at special risk include those with impaired pulmonary function, especially those with obstructive airway diseases, since the breathing of copper fume might cause exacerbation of symptoms due to its irritant properties.

Substance	Hepatotoxic
<b>Copper Fume</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system (*increased risk with Wilson's disease*).
2. HSDB Medical Surveillance: Consider the skin, eyes, and respiratory system in any placement or periodic examinations. Copper and compounds approximately 1 in 200,000 individuals has inherited a pair of abnormal genes, as a result of which copper toxicosis (Wilson's disease) will ultimately develop. This will occur with the ingestion of only a normal diet containing 2-5 mg of copper/day and will probably occur more rapidly and more severely if the individual inhales or ingests more of the metal by working in a copper mine. The disease is progressive and fatal if untreated by a de-coppering regimen. Screening in employment health examination to exclude the employment of persons suffering from this condition could be accomplished by determining the serum concern of ceruloplasmin quantitatively since normal individuals have from 20-50 mg/cu cm of this copper protein whereas 97% of patients with Wilson's disease have less than 20 mg/100 cu cm.
3. HSDB Populations at Special Risk: Persons at special risk include those with impaired pulmonary function, especially those with obstructive airway diseases, since the breathing of copper fume might cause exacerbation of symptoms due to its irritant properties.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Cresol*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, **liver**, kidneys, pancreas, cardiovascular system.
2. HSDB Medical Surveillance: It is recommended that a preplacement medical examinations should include at least: a urinalysis that includes a microscopic examination. Additional tests, such as complete blood counts and **liver** and kidney function tests, should be considered by the responsible physician. An evaluation of the worker's ability to use positive and negative pressure respirators. Periodic examinations shall be made available on at least an annual basis. These examinations should include interim medical and work histories. Employees complaining of skin abnormalities, such as scaling, crusting, or irritation, that may be attributed to exposure to cresol shall be medically evaluated. Pertinent medical records shall be maintained by the employer for all employees occupationally exposed to cresol. Such records shall be retained for at least 30 years after termination of employment. Records of environmental exposures applicable to an employee shall be included in the employee's medical records. These records shall be made available to the designated medical representatives. In cases of splashes, spills, or leaks where significant skin or eye contact with, or inhalation of the material occurs, appropriate medical personnel shall be notified. Medical attendants shall be informed of the possibility of delayed systemic effects, and the persons so exposed shall be observed for a minimum of 72 hours. Medical examinations shall be made available as warranted by the results of the 72 hour observation period.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Cyanides</b>	<b>N</b>

1. IRIS Critical Effects: Rat Chronic Oral Study - Howard and Hanzal, 1955. Weight loss, thyroid effects and myelin degeneration. Rat Subchronic to Chronic Oral Bioassay - Philbrick et al., 1979.
2. Hepatotoxicity may occur as a secondary effect (primary effect on respiration).

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Cyclohexane</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
2. HSDB Medical Surveillance: Biological monitoring of cyclohexane via alveolar air and urine can be reliably used in the evaluation of occupational exposure.
3. HSDB Populations at Special Risk: Individuals with a history of kidney, **liver**, respiratory, or skin problems.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Cyclohexanol</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Cyclohexanone*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, **liver**, kidneys.
2. HSDB Toxic Hazard Rating: Evaluation: There is inadequate evidence for the carcinogenicity of cyclohexanone in experimental animals. No data were available from studies in humans on the

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

carcinogenicity of cyclohexanone. Overall evaluation: Cyclohexanone is not classifiable as to its carcinogenicity to humans.

3. HSDB Medical Surveillance: Consider the points of attack respiratory system, eyes, skin, central nervous system in preplacement and periodic physical examinations.

Substance	Hepatotoxic
<b>Cyclopentadiene</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
2. HSDB Medical Surveillance: Consider the points of attack eyes, respiratory system in placement and periodic physical examinations.

Substance	Hepatotoxic
<b>Dibutyl Phosphate</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system.

Substance	Hepatotoxic
<b>Dibutylphthalate</b>	N

1. IRIS Critical Effects: Increased mortality. Rat Subchronic to Chronic Oral Bioassay - Smith, 1953.
2. NIOSH Target Organs: Eyes, respiratory system, gastrointestinal tract.
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: Pertinent data regarding carcinogenicity was not located in the available literature. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.
4. HSDB Medical Surveillance: Routine medical examinations should be provided to each employee who is exposed to dibutyl phthalate at potentially hazardous levels.

Substance	Hepatotoxic
<b>o-Dichlorobenzene*</b>	Y

1. IRIS Critical Effects: No adverse effects observed. 2-Year Rat Study, Oral Exposure (gavage) - NTP, 1985.
2. NIOSH Target Organs: Eyes, respiratory system, liver, kidneys.
3. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) evidence in humans: inadequate; 2) evidence in animals: inadequate. Overall summary evaluation of carcinogenic risk to humans is group 3: The agent is not classifiable as to its carcinogenicity to humans. EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: Based on no human data and evidence of both negative and positive trends for carcinogenic responses in rats and mice. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.
4. HSDB Medical Surveillance: Employees should be screened for history of liver, kidney, or skin disease, which might place the employee at increased risk from o-dichlorobenzene exposure.

5. HSDB Populations at Special Risk: Persons with existing pathology (hepatic, renal, central nervous system, blood), or metabolic disorders, who are taking certain drugs (hormones, or otherwise metabolically active) or who are otherwise exposed to dichlorobenzenes or to related (chemically or biologically) chemicals, by such means as occupation or domestic use or abuse might well be considered at increased risk from exposure to dichlorobenzenes.

Substance	Hepatotoxic
<b>p-Dichlorobenzene*</b>	<b>Y</b>

1. IRIS Critical Effects: Increased liver weights in P1 males. Rat Multigeneration Reproductive Study - Chlorobenzene Producers Assn., 1986.

2. NIOSH Target Organs: Liver, respiratory system, eyes, kidneys, skin (*in animals; liver and kidney cancer*).

3. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) evidence in humans: inadequate; 2) evidence in animals: sufficient. Overall summary evaluation of carcinogenic risk to humans is group 2B: The agent is possibly carcinogenic to humans. A3. A3= Animal carcinogen.

4. HSDB Medical Surveillance: Amount of 2,5-DICHLOROPHENOL present in urine can serve as indication of exposure and physical examination: The purpose is to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the liver, respiratory tract, eyes, and kidneys should be stressed. The skin should be examined for evidence of chronic disorders. PRECAUTIONS FOR "CARCINOGENS": in relation specifically to cancer hazards, there are at present no health monitoring methods that may ensure the early detection of preneoplastic lesions or lesions which may precede them. Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning additional tests that might become useful or mandatory.

5. HSDB Populations at Special Risk: Persons with existing pathology (hepatic, renal, central nervous system, blood), or metabolic disorders, who are taking certain drugs (hormones, or otherwise metabolically active) or who are otherwise exposed to dichlorobenzenes or to related (chemically or biologically) chemicals, by such means as occupation or domestic use or abuse might well be considered at increased risk from exposure to dichlorobenzenes.

Substance	Hepatotoxic
<b>Dichlorodifluoromethane (Freon 12)</b>	<b>N</b>

1. NIOSH Target Organs: Cardiovascular system, peripheral nervous system.

2. HSDB Medical Surveillance: Employees should be screened for history of certain medical conditions which might place the employee at increased risk from dichlorodifluoromethane exposure. Cardiovascular disease: In persons with impaired cardiovascular function, especially those with a history of cardiac arrhythmias, the inhalation of dichlorodifluoromethane might cause exacerbation of disorders of the conduction mechanism due to its sensitizing effects on the myocardium. Any employee developing the above-listed conditions should be referred for further medical examination.

3. HSDB Populations at Special Risk: Employees with cardiovascular disease are at increased risk. In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of Refrigerant 114 might cause exacerbation of symptoms due to its irritant properties. In persons with impaired cardiovascular function, especially those with history of cardiac arrhythmias, the inhalation of Refrigerant 114 might cause exacerbation of disorders of the conduction mechanism due to sensitizing effects on the myocardium.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>1,1-Dichloroethane*</b>	<b>Y</b>

1. IRIS: Evidence for classification as to human carcinogenicity: WEIGHT-OF-EVIDENCE CLASSIFICATION: C; possible human carcinogen. Basis: Based on no human data and limited evidence of carcinogenicity in two animal species (rats and mice) as shown by an increased incidence of mammary gland adenocarcinomas and hemangiosarcomas in female rats and an increased incidence of hepatocellular carcinomas and benign uterine polyps in mice. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Limited. An NCI bioassay (1978a) provides limited evidence of the carcinogenicity of 1,1-dichloroethane in Osborne-Mendel rats and B6C3F1 mice. This is based on significant dose-related increases in the incidence of hemangiosarcomas at various sites and mammary carcinomas in female rats and statistically significant increases in the incidence of liver carcinoma in male mice and benign uterine polyps in female mice. The study is limited by high mortality in many groups; the low survival rates precluded the appearance of possible late-developing tumors and decreased the statistical power of this bioassay.

2. NIOSH Target Organs: Skin, liver, kidneys, lungs, CNS.

3. HSDB Medical Surveillance: 1. The following medical procedures should be made available to each employee who is exposed to 1,1-dichloroethane at potentially hazardous levels: Initial Medical Screening: Employees should be screened for history of certain medical conditions which might place the employee at increased risk from 1,1-dichloroethane exposure. Skin disease: 1,1-Dichloroethane can cause dermatitis on prolonged exposure. Persons with existing skin disorders may be more susceptible to the effects of this agent. Liver disease: Although 1,1-dichloroethane is not known as a liver toxin in humans, the importance of this organ in the biotransformation and detoxification of foreign substances should be considered before exposing persons with impaired liver function. Kidney disease: Although 1,1-dichloroethane is not known as a kidney toxin in humans, the importance of this organ in the elimination of toxic substances justifies special consideration in those with impaired renal function. Chronic respiratory disease: In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of 1,1-dichloroethane might cause exacerbation of symptoms due to its irritant properties. Periodic Medical Examination: Any employee developing the above-listed conditions should be referred for further medical examination.

4. HSDB Populations at Special Risk: 1. Persons with existing skin disorders may be more susceptible to the effects of this agent. Chronic respiratory disease: In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of 1,1-dichloroethane might cause exacerbation of symptoms due to its irritant properties.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>1,2-Dichloroethane</b>	<b>Y</b>

1. IRIS: EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY: 1. WEIGHT-OF-EVIDENCE CLASSIFICATION: B2; probable human carcinogen. Basis: Based on the induction of several tumor types in rats and mice treated by gavage and lung papillomas in mice after topical application. 2. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: 1,2-Dichloroethane in corn oil was administered by gavage to groups of 50 each male and female Osborne-Mendel rats and B6C3F1 mice. Treatment was for 78 weeks followed by an additional observation period of 12-13 weeks for mice or 32 weeks for low-dose rats. TWA dosages were 47 and 95 mg/kg/day for rats, 97 and 195 mg/kg/day for male mice and 149 and 299 mg/kg/day for female mice. All high-dose male rats died after 23 weeks of observation; the last high-dose female died after 15 weeks. Male rats had significantly increased incidence of forestomach squamous-cell carcinomas and circulatory system hemangiosarcomas. Female rats and mice were observed to have significant increases in mammary adenocarcinoma incidence. Mice of both sexes developed alveolar/bronchiolar adenomas,

females developed endometrial stromal polyps and sarcomas, and males developed hepatocellular carcinomas (NCI, 1978). Inhalation exposure of Wistar, Sprague-Dawley rats and Swiss mice did not result in increased tumor incidence (Spencer et al., 1951; Maltoni et al., 1980). An elevation that was not statistically significant in lung adenomas was seen in A/st mice treated i.p. with 1,2-dichloroethane in tricaprylin (Theiss et al., 1977). ICR/Ha Swiss mice treated topically had a significant increase in benign lung papillomas, but not skin carcinomas (van Duuren et al., 1979).

2. HSDB Medical Surveillance: 1. Annual medical exams shall be made available to all workers exposed to ethylene dichloride including medical and work history and comprehensive medical exam with particular attention to cardiovascular, pulmonary, neurological, liver and kidney functions. Records will be maintained for 20 yrs after termination of employment. 2. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning /cytogenetic and/or other tests that might become useful or mandatory.
3. HSDB Populations at Special Risk: 1. Nursing mothers should not be exposed to 1,2-dichloroethane.

Substance	Hepatotoxic
<b>Dichloromonofluoromethane (Freon 21, Halon 112)</b>	<b>N</b>

1. NIOSH Target Organs: Respiratory system, cardiovascular system.
2. HSDB Medical Surveillance: Consider the points of attack respiratory system, lung, cardiovascular system in preplacement and periodic physical examinations.
3. HSDB Populations at Special Risk: It is possible that pt with cardiac or respiratory disorders may prove especially susceptible.

Substance	Hepatotoxic
<b>Dichlorotetrafluoroethane (Freon 114)</b>	<b>N</b>

1. NIOSH Target Organs: Respiratory system, cardiovascular system.
2. HSDB Medical Surveillance: Initial Medical Screening: Employees should be screened for history of certain medical conditions which might place the employee at increased risk from Refrigerant 114 exposure. These are chronic respiratory and cardiovascular disease. Periodic Medical Examination: Any employee developing these conditions should be referred for further medical examination.
3. HSDB Populations at Special Risk: It is possible that patients with cardiac or respiratory disorders may prove especially susceptible to aerosol propellants. In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of Refrigerant 114 might cause exacerbation of symptoms due to its irritant properties. In persons with impaired cardiovascular function, especially those with history of cardiac arrhythmias, the inhalation of Refrigerant 114 might cause exacerbation of disorders of the conduction mechanism due to sensitizing effects on the myocardium.

Substance	Hepatotoxic
<b>Dichlorvos (Pesticide)</b>	<b>N</b>

1. IRIS Critical Effects: Plasma and RBC ChE inhibition in males and females; brain ChE inhibition in males. 1-Year Dog Feeding Study - AMVAC Chemical Corp., 1990 - Decrease brain cholinesterase activity. Carworth Farm E Strain Rat Chronic Inhalation Study - Blair et al., 1976.

2. NIOSH Target Organs: Respiratory system, cardiovascular system, central nervous system, eyes, skin, blood cholinesterase.

3. HSDB Toxic Hazard Rating: Evaluation: There is inadequate evidence in humans for the carcinogenicity of dichlorvos. There is sufficient evidence in experimental animals for the carcinogenicity of dichlorvos. Overall evaluation: Dichlorvos is possibly carcinogenic to humans (2B). EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Significant increases in forestomach tumors in female and male B6C3F1 mice and leukemias and pancreatic acinar adenomas in Fischer 344 rats. Supporting evidence included observation of tumors at other sites in the rat and observation of mutagenicity for both dichlorvos and a major metabolite dichloroacetaldehyde. A structurally related material, dichloropropene, also induces forestomach tumors in rodents. NOTE: The carcinogen assessment for dichlorvos may change in the near future pending the outcome of a further review being conducted by the CRAVE Work Group. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Sufficient.

4. HSDB Medical Surveillance: A complete history and physical examination. Examination of the respiratory system, nervous system, cardiovascular system, and attention to the cholinesterase levels in the blood should be stressed. The skin should be examined for chronic disorders. The cholinesterase activity in the serum and erythrocytes should be determined by using acceptable biochemical tests prior to any new period of exposure. Medical examinations should be repeated on annual basis, with the exception of cholinesterase determination which should be performed quarterly or at any time overexposure is suspected or signs or symptoms of toxicity occur. Workers must undergo an annual medical exam at the beginning of each agricultural season. Contraindications for work with organophosphorus pesticides are organic diseases of the CNS, mental disorders & epilepsy, pronounced endocrine & vegetative disorders, pulmonary tuberculosis, bronchial asthma, chronic respiratory diseases, cardiovascular diseases and circulatory disorders, gastrointestinal diseases (peptic ulcer), gastroenterocolitis, diseases of the liver & kidneys, eye diseases (chronic conjunctivitis and keratitis). Blood cholinesterase activity must be determined before work starts. In the event of prolonged work periods, this activity should be determined at intervals of 3-4 days. Persons exhibiting a fall in cholinesterase activity of 25% or more must be transferred to other work where they are not exposed until cholinesterase level is completely restored.

5. HSDB Populations at Special Risk: Persons with a history of reduced pulmonary function, convulsive disorders, or recent exposure to anticholinesterase agents would be expected to be at increased risk from exposure. Dichlorvos is rapidly inactivated by liver enzymes. Patients with hepatic insufficiency may be less tolerant to the toxic effects of dichlorvos. Work must not be carried out by young persons under 18 yr, expectant or nursing mothers, or persons for whom work with toxic chemicals is contraindicated on account of their state of health; the same applies to alcoholics. Contraindications for work with organophosphorus pesticides are organic diseases of the CNS, mental disorders & epilepsy, pronounced endocrine & vegetative disorders, pulmonary tuberculosis, bronchial asthma, chronic respiratory diseases, cardiovascular diseases and circulatory disorders, gastrointestinal diseases (peptic ulcer), atroenterocolitis, diseases of the liver & kidneys, eye diseases (chronic conjunctivitis and keratitis).

Substance	Hepatotoxic
Dieldrin*	Y

1. IRIS Critical Effects: Liver lesions. 2-Year Rat Feeding Study - Walker et al., 1969.

2. NIOSH Target Organs: Central nervous system, liver, kidneys (*in animals: lung, liver, thyroid and adrenal gland tumors*).

3. HSDB Toxic Hazard Ratings: EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Dieldrin is carcinogenic in seven strains of mice when administered orally. Dieldrin is structurally related to compounds (aldrin, chlordane, heptachlor, heptachlor epoxide, and chlorendic acid)

which produce tumors in rodents. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient. Classification of carcinogenicity: 1) evidence in humans: inadequate; 2) evidence in animals: inadequate; 3) evidence for activity in short-term tests: limited. Summary evaluation of carcinogenic risk to humans 3: The chemical cannot be classified as to its carcinogenicity to humans.

4. HSDB Medical Surveillance: Consider the points of attack central nervous system, **liver**, kidneys, skin in preplacement and periodic physical exam. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and/or other tests that might become useful or mandatory.

Substance	Hepatotoxic
<b>Diethylamine</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system, cardiovascular system.
2. HSDB Toxic Hazard Ratings: A4. A4= Not Classifiable as a Human Carcinogen.
3. HSDB Medical Surveillance: Employee who is exposed to diethylamine at potentially hazardous levels should be screened for history of certain medical conditions (skin, eye, chronic respiratory diseases) which might place the employee at increased risk from diethylamine exposure. Any employee developing these conditions should be referred for further medical exam.

Substance	Hepatotoxic
<b>Dimethylamine</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system.
2. HSDB Medical Surveillance: Employee who is exposed to dimethylamine at potentially hazardous levels should be screened for history of certain medical conditions (skin, eye, chronic respiratory diseases) which might place the employee at increased risk from dimethylamine exposure. Any employee developing the conditions should be referred for further medical exam.

Substance	Hepatotoxic
<b>Dimethylformamide*</b>	Y

1. IRIS Critical Effects: Digestive disturbances and minimal hepatic changes suggestive of **liver** abnormalities. Human Occupational Studies - Cirla et al., 1984; Catenacci et al., 1984.
2. NIOSH Target Organs: Eyes, skin, respiratory system, **liver**, kidneys, cardiovascular system.
3. HSDB Toxic Hazard Rating: Evaluation: There is limited evidence for the carcinogenicity of dimethylformamide in humans. There is inadequate evidence for the carcinogenicity of dimethylformamide in experimental animals. Overall evaluation: Dimethylformamide is possibly carcinogenic to humans (Group 2B).
4. HSDB Medical Surveillance: Preplacement and periodic examinations should be concerned particularly with **liver** and kidney function and with possible effects on the skin. The determination of a dimethylformamide metabolite, methylformamide, in the urine of exposed workers has been recommended as a guide to monitoring worker exposure. The fluctuation in the rate of excretion of this metabolite requires that methylformamide determinations be carried out on 24 hr urine specimens. The 24 hr urinary

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

excretion of 50 mg or less of methylformamide is consistent with occupational exposure to 20 ppm of dimethylformamide vapor.

5. HSDB Populations at Special Risk: Investigations show that dimethylformamide, despite its relatively low vapor pressure, affects most workman handling it, especially those suffering from gastric or liver troubles (ulcers, gastritis, alcoholism).

Substance	Hepatotoxic
<b>Dimethylphthalate</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, respiratory system, gastrointestinal tract.
2. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: Pertinent data regarding carcinogenicity data was not located in the available literature. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.
3. HSDB Medical Surveillance: Routine medical examinations should be provided to each employee who is exposed to dimethyl phthalate at potentially hazardous levels. Consider the routes of exposure in preplacement and periodic physical examinations.

Substance	Hepatotoxic
<b>Endrin (Pesticide)*</b>	<b>Y</b>

1. IRIS Critical Effects: Mild histological lesions in liver, occasional convulsions. Dog Chronic Oral Bioassay - Velsicol Chemical Corp. 1969
2. NIOSH Target Organs: Central nervous system, liver.
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to carcinogenicity for humans. Basis for Classification: Oral administration of endrin did not produce carcinogenic effects in either sex of two strains of mice. An NCI bioassay was suggestive of responses in male and female rats although NCI reported a no evidence conclusion. The inadequacies of the several bioassays call into question the strength of the reported negative findings. These inadequacies and the suggestive responses in the NCI bioassay do not support a Group E classification; rather a Group D classification best reflects the equivocal data. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Inadequate. No data are available in humans. Inadequate evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans.
4. HSDB Medical Surveillance: Initial Medical Examination: A complete history and physical examination: The purpose is to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Persons with a history of convulsive disorders would be expected to be at increased risk from exposure. Examination of the nervous system and liver should be stressed. The concentration of endrin in the blood is helpful in determining the extent of absorption. The aforementioned medical examination should be repeated on an annual basis.
5. HSDB Populations at Special Risk: Agricultural workers, home gardeners, and those involved in endrin manufacture and distribution, especially when measuring and pouring the emulsifiable concentrated material, are at increased risk to mostly dermal and some respiratory exposures. Pregnant women, particularly those whose diets contain large amounts of fish, are considered a special group at risk. Evidence that endrin may cause chromosomal damage in germinal tissue suggests that men and

women of child-bearing age may also be a special risk group. Persons with a history of convulsive disorders would be expected to be at increased risk from exposure to endrin.

Substance	Hepatotoxic
<b>Epichlorohydrin*</b>	<b>Y</b>

1. IRIS Critical Effects: Changes in the nasal turbinates. Rat and Mouse 90-Day Inhalation Study - Quast et al., 1979a.
2. NIOSH Target Organs: Eyes, skin, respiratory system, kidneys, **liver**, reproductive system (*in animals; nasal cancer*). NIOSH concluded that risks from exposure to epichlorohydrin may include carcinogenesis, mutagenesis, and sterility, as well as damage to the kidneys, **liver**, respiratory tract and skin.
3. HSDB Toxic Hazard Rating: 1. EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Human data are inadequate. Multiple studies in rats and mice administered epichlorohydrin by various routes were positive. As epichlorohydrin is a strong alkylating agent, tumors are produced at the site of application. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient.
4. HSDB Medical Surveillance: There have been no cases of serious pulmonary injury or systemic toxicity in manufacturing or handling of epichlorohydrin. Because of potential nephrotoxic effects, persons working with this material on a continuing basis should undergo medical supervision.

Substance	Hepatotoxic
<b>2-Ethoxyethanol (Ethylene Glycol Monoethyl Ether)*</b>	<b>Y</b>

1. IRIS Critical Effects: Decreased testis weight, seminiferous tubule degeneration and decrease hemoglobin. New Zealand Whit Rabbit Subchronic Toxicity Study - Barbee et al., 1984.
2. NIOSH Target Organs: Eyes, respiratory system, blood, kidneys, **liver**, reproductive system, hematopoietic system.

Substance	Hepatotoxic
<b>2-Ethoxyethyl Acetate (Cellosolve Acetate, Ethylene Glycol Monoethyl Ether Acetate)</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, respiratory system, gastrointestinal tract, reproductive system, hematopoietic system.
2. HSDB Medical Surveillance: Consider the points of attack respiratory system, eyes, gastrointestinal system in placement and periodic physical examinations.

Substance	Hepatotoxic
<b>Ethyl Acetate</b>	<b>N</b>

1. IRIS Critical Effects: Mortality and body weight loss. Rat Oral Subchronic Study - U.S. EPA 1986.
2. NIOSH Target Organs: Eyes, skin, respiratory system.
3. HSDB Medical Surveillance: Consider the points of attack eyes, skin, respiratory system in placement and periodic examinations.

4. HSDB Populations at Special Risk: Employees with chronic respiratory, skin, liver, or kidney disease may be at increased risk from ethyl acetate.

Substance	Hepatotoxic
Ethylamine	N

1. NIOSH Target Organs: Eyes, skin, respiratory system.

2. HSDB Medical Surveillance: Consider the points of attack respiratory system, eyes, skin in placement and periodic physical exam.

Substance	Hepatotoxic
Ethylbenzene	N

1. IRIS Critical Effects: Developmental toxicity. Rat and Rabbit Developmental Inhalation Studies - Andrew et al., 1981 - Hardin et al., 1981. Liver and kidney toxicity - Wolf et al., 1956.

2. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.

3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: nonclassifiable due to lack of animal bioassays and human studies. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.

4. Potential for Interactions: In rats, the ability of ethylbenzene to modify the metabolism of other potentially toxic substances in liver, kidney, and lung microsomes suggested the possibility of synergistic toxic responses.

5. HSDB Medical Surveillance: Employment examinations should ensure that persons with liver, kidney nervous system, blood and hemopoietic organ disorders are not exposed. Exposure of women with ovulation and menstrual cycle disorders should also be prevented. Consider the points of attack (eyes, upper respiratory system, skin, central nervous system) in placement and periodic physical examination.

6. HSDB Populations at special risk: In persons with impaired pulmonary function, especially those with obstructive airway diseases, breathing ethyl benzene might cause exacerbation of symptoms due to its irritant properties or psychic reflex bronchosp. Persons with existing skin disorders may be more susceptible to effects. Persons with liver, kidney, nervous system, blood and hemopoietic organ disorders. Woman with ovulation and menstrual cycle disorders.

Substance	Hepatotoxic
Ethylenediamine*	Y

1. NIOSH Target Organs: Skin, respiratory system, liver, kidneys.

2. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: Based on no human data and inadequate animal data. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.

3. HSDB Medical Surveillance: A complete history and physical exam is required to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Persons with a history of asthma, allergies, or unknown sensitization to ethylenediamine would be expected to be at increased risk from exposure. Exam of the resp system, liver, and kidneys should be stressed. The skin should be examined for evidence of chronic disorders should be repeated on an annual basis.

4. HSDB Populations at Special Risk: Persons with a history of asthma, allergies, or unknown sensitization to ethylenediamine are at increased risk from exposure.

Substance	Hepatotoxic
<b>Ethylene Dibromide*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, **liver**, kidneys, reproductive system (*in animals; skin and lung cancer*).
2. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: B2; probable human carcinogen. BASIS FOR CLASSIFICATION: Increased incidences of a variety of tumors in rats and mice in both sexes by three routes of administration at both the site of application and at distant sites. EDB is mutagenic in various *in vitro* and *in vivo* assays. EDB is structurally similar to DBCP, a probable human carcinogen and to EDC, a probable human carcinogen. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient. A2, skin. A2= Suspected human carcinogen.
3. HSDB Medical Surveillance: The following medical procedures should be made available to each employee who is exposed to ethylene dibromide at potentially hazardous levels. Initial medical examination: A complete history and physical examination: The purpose is to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the nervous and respiratory systems, heart, **liver**, and kidneys should be stressed. The skin should be examined for evidence of chronic disorders. A 14" by 17" chest roentgenogram: Ethylene dibromide causes human lung damage. Surveillance of the lung is indicated. Forced vital capacity and forced expiatory volume (1 sec): Ethylene dibromide is a respiratory irritant. Liver function tests: Ethylene dibromide may cause **liver** damage. A profile of **liver** function should be obtained by utilizing a medically acceptable array of biochemical tests. Cardiacfunction: An electrocardiogram should be performed on workers over 40 years of age and where indicated. Skin: Ethylene dibromide is a defatting agent and can cause dermatitis. Periodic Medical Examination: The aforementioned examinations should be repeated on an annual basis. \*\* PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.
4. HSDB Populations at Special Risk: Individuals with diseases of **liver** and kidney. Individuals who may be at risk from exposure to ethylene dibromide include those with impaired pulmonary function; individuals with **liver**, skin, kidney, and cardiovascular diseases. Pregnant women may also be at increased risk from exposure to ethylene dibromide.

Substance	Hepatotoxic
<b>Ethylene Oxide*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, **liver**, central nervous system, blood, kidneys, reproductive system (*peritoneal cancer, leukemia*).
2. HSDB Toxic Hazard Rating: Individuals who may be at risk from exposure to ethylene dibromide include those with impaired pulmonary function; individuals with **liver**, skin, kidney, and cardiovascular diseases. Pregnant women may also be at increased risk from exposure to ethylene dibromide.
3. HSDB Medical Surveillance: Biological monitoring of ethylene oxide exposure by analysis of alveolar air and blood was studied in 10 workers employed in a hospital sterilizer unit. Environmental air, alveolar air, and venous blood were sampled during and at the end of an 8 hr workshift. The mean environmental concentration of ethylene oxide was 5.4 mg/cu m air and the mean alveolar ethylene oxide concentration was 1.2 mg/cu m alveolar air. Regression analysis showed that blood ethylene oxide

concentrations were higher than environmental ethylene oxide concentrations by a mean ratio of 3 and higher than alveolar ethylene oxide concentrations by a mean ratio of 12. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.

4. HSDB Populations at Special Risk: Ethylene oxide is a suspected occupational toxicant of the male reproductive system indigenous to the occupation of hospital sterilizers. Industrial and occupational exposure is generally the result of inhalation of ethylene oxide vapor released from leaking or faulty equipment, valves, or fittings. Hospital workers operating a defective ethylene oxide sterilizer.

Substance	Hepatotoxic
Ethyl Mercaptan*	Y

1. NIOSH Target Organs: Eyes, respiratory system, liver, kidneys, blood.
2. HSDB Medical Surveillance: Prior to placing a worker in a job with a potential for exposure to ethyl mercaptan, the physician should evaluate and document the worker's baseline health status with thorough medical, environmental, and occupational histories, a physical examination, and physiologic and laboratory tests appropriate for the anticipated occupational risk. These should concentrate on the function and integrity of the nervous and respiratory systems. Medical surveillance for respiratory disease should be conducted by using the principles and methods recommended by NIOSH and the American Thoracic Society (ATS). A preplacement medical evaluation is recommended in order to detect and assess preexisting or concurrent conditions which may be aggravated or result in increased risk when a worker is exposed to n-butyl mercaptan at or below the NIOSH REL. The examining physician should consider the probable frequency, intensity, and duration of exposure, as well as the nature and degree of the condition, in placing such a worker. Such conditions, which should not be regarded as absolute contraindications to job placement, include chronic diseases of the respiratory system.

Substance	Hepatotoxic
Fluorides	N

1. No information was obtained from IRIS or NIOSH Pocket Guide to Chemical Hazards.

Substance	Hepatotoxic
Formaldehyde	N

1. IRIS Critical Effects: Reduced weight gain, histopathology in rats. Rat 2-Year Bioassay - Til et al., 1989.
2. NIOSH Target Organs: Eyes, respiratory system (*nasal cancer*).
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: B1; probable human carcinogen. Basis for Classification: Based on limited evidence in humans, and sufficient evidence in animals. Human data include nine studies that show statistically significant associations between site-specific respiratory neoplasms and exposure to formaldehyde or formaldehyde-containing products. An increased incidence of nasal squamous cell carcinomas was observed in long-term inhalation studies in rats and in mice. The classification is supported by *in vitro* genotoxicity data and formaldehyde's structural relationships to other carcinogenic aldehydes such as acetaldehyde. HUMAN CARCINOGENICITY DATA: Limited. ANIMAL CARCINOGENICITY DATA: Sufficient. A2. A2= Suspected human carcinogen.
4. HSDB Populations at Special Risk: Mean formaldehyde levels are highest in hospital autopsy rooms compared with other commercial settings. Hospital autopsy workers are possibly exposed. Release of

formaldehyde vapors in mobile homes has been associated with headache and pulmonary and dermal irritation. Occupants of mobile homes are possibly exposed.

Substance	Hepatotoxic
<b>Heptachlor*</b>	<b>Y</b>

1. IRIS Critical Effects: **Liver** weight increases, increases in males. 2-Year Rat Feeding Study - Velsicol Chemical, 1955a.
2. NIOSH Target Organs: Central nervous system, **liver** (*in animals; liver cancer*).
3. HSDB Toxic Hazard Rating: Evaluation: There is inadequate evidence in humans for the carcinogenicity of heptachlor. There is sufficient evidence in experimental animals for the carcinogenicity of heptachlor. Overall evaluation: Heptachlor is possibly carcinogenic to humans (2B). EPA CLASSIFICATION: B2; probable human carcinogen. Basis for Classification: Inadequate human data, but sufficient evidence exists from studies in which benign and malignant **liver** tumors were induced in three strains of mice of both sexes. Several structurally related compounds are **liver** carcinogens. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient. A3. A3= Animal Carcinogen.
4. HSDB Medical Surveillance: A complete history and physical examination: The purpose is to detect preexisting conditions that might place the employee at an increased risk, and to establish a baseline for future health monitoring. Examination of the eyes, nervous system, **liver**, and kidneys should be stressed. The aforementioned medical examination should be repeated on an annual basis. Protect from exposure those individuals with diseases of kidney, **liver**, and lung. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.
5. HSDB Populations at Special Risk: Preclude from exposure those individuals with convulsive disorders.

Substance	Hepatotoxic
<b>n-Heptane</b>	<b>N</b>

1. NIOSH Target Organs: Skin, respiratory system, central nervous system.
2. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: No human data and no animal data available. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.
3. HSDB Populations at Special Risk: Persons with preexisting skin disorders may be more susceptible to the effects of this agent. In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of heptane might cause exacerbation of symptoms due to its irritant properties.

Substance	Hepatotoxic
<b>n-Hexane</b>	<b>N</b>

1. IRIS Critical Effects: Neurotoxicity: Electrophysiological alterations. Epidemiological Inhalation Study - Sanagi et al., 1980 Epithelial lesions in the nasal cavity. 90-Day Mouse Inhalation Study - Dunnick et al., 1989.

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

2. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, peripheral nervous system.

Substance	Hepatotoxic
<b>2-Hexanone (MBK)</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, peripheral nervous system.

2. **Interactions are a potential problem.** Compounds which induce liver microsomal enzymes, such as widely used methyl ethyl ketone & phenobarbital, increase blood levels of 2,5-hexanediol & neurotoxicity of MBK.

Substance	Hepatotoxic
<b>Hexone (MIBK)*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, liver, kidneys.

2. HSDB Medical Surveillance: Preplacement medical evaluations should emphasize target organs: respiratory system, eyes, skin, central nervous system.

3. An experiment was conducted to investigate the mechanism of methyl isobutyl ketone synergism of n-hexane neurotoxicity. The results suggest that the synergistic action of methyl isobutyl ketone on n-hexane neurotoxicity may be related to its ability to induce liver microsomal cytochrome P450, resulting in increased metabolic activation of n-hexane to more potent neurotoxic metabolites.

Substance	Hepatotoxic
<b>Hydrazine*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, liver, kidneys (*in animals; tumors of the lungs, liver, blood, vessels and intestine*).

2. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) evidence in humans: inadequate; 2) evidence in animals: sufficient; 3) evidence for activity in short term tests: sufficient. Summary evaluation of carcinogenic risk to humans 2B: Inadequate evidence that the chemical is carcinogenic to humans.

3. HSDB Medical Surveillance: Based partly on exptl data, placement should include a history of exposure to other carcinogens, smoking, alcohol, medications, & family history. The skin, eye, liver, kidney, blood & CNS should be evaluated. Sputum or urine cytology may give useful information. Hydrazine may be detected in blood.

Substance	Hepatotoxic
<b>Hydrogen Cyanide</b>	<b>N</b>

1. IRIS Critical Effects: Rat Chronic Oral Study - Howard and Hanzal, 1955 Weight loss, thyroid effects, and myelin degeneration. Rat Subchronic to Chronic Oral Bioassay - Philbrick et al., 1979 Central nervous system symptoms and thyroid effects. Occupational Study - El Ghawabi et al., 1975

2. NIOSH Target Organs: Central nervous system, cardiovascular system, thyroid, blood.

3. Points of attack: Liver, kidneys, cardiovascular system, central nervous system.

4. Hepatic effects are secondary effects. The liver contains the highest activity of rhodanese, therefore it is possible that existing liver disease might slow the rate of cyanide metabolism..
5. HSDB Medical Surveillance: Pre-placement and periodic examinations should include the cardiovascular and central nervous systems, liver and kidney function, blood, history of fainting and dizzy spells. Blood cyanide levels may be useful during acute intoxication. Urinary thiocyanate levels have been used but are nonspecific and are elevated in smokers. Initial medical examination /should include/: a complete history and physical examination to detect existing conditions that might place the exposed employee at increased risk & to establish a baseline for future health monitoring. Examination of cardiovascular, nervous, & upper resp systems, & thyroid should be stressed. The skin should be exam for evidence of chronic disorders. The aforementioned medical exam should be repeated on an annual basis.
6. HSDB Populations at Special Risk: Workers with chronic diseases of kidneys, respiratory tract, skin, or thyroid are at greater risk of developing toxic cyanide effects than are healthy workers.

Substance	Hepatotoxic
<b>Hydrogen Fluoride</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, bones.
2. HSDB Medical Surveillance: Physical examinations of exposed personnel every six months including fluoride determinations in urine, studies of liver and kidney function; chest X-ray, annually. Protect from exposure those individuals with diseases of kidneys, liver, and lung.

Substance	Hepatotoxic
<b>Hydrogen Peroxide</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system.
2. HSDB Toxic Hazard Rating: No data are available in humans. Limited evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans.

Substance	Hepatotoxic
<b>Hydrogen Sulfide</b>	<b>N</b>

1. IRIS Critical Effects: Gastrointestinal disturbance. Pig Oral Toxicity Study (Subchronic) - Watterau et al., 1964 Inflammation of the nasal mucosa. Mouse Subchronic Inhalation Study - CIIT 1983a
2. NIOSH Target Organs: Eyes, respiratory system, central nervous system.
3. HSDB Medical Surveillance: Analysis of reticulocytes for delta-amino-levulinic acid synthase (amlev synthase) and heme synthase activity in 17 workers in pulp production with low-level hydrogen sulfide and methylmercaptan exposure showed decreased activities in 8 and 6 cases respectively. The assay of amlev synthase and heme synthase could be a valuable addition to the assessment of workers' health in industries generating hydrogen sulfide. Placement medical examinations should evaluate any existing neurological, eye and respiratory conditions and any history of fainting seizures. It is recommended by NIOSH that placement and periodic examinations (once every 3 years) be made available to all workers occupationally exposed to hydrogen sulfide.

**Substance** **Hepatotoxic**  
**Hydroquinone** **N**

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.

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**Substance** **Hepatotoxic**  
**Isoamyl Acetate** **N**

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
2. HSDB Medical Surveillance: Initial Medical Screening: Employees should be screened for history of chronic respiratory, skin, kidney, or liver diseases which might place the employee at increased risk from isoamyl acetate exposure. Periodic Medical Examination: Any employee developing the above-listed conditions should be referred for further medical examination.
3. HSDB Populations at Special Risk: In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of isoamyl acetate might cause exacerbation of symptoms due to its irritant properties. Persons with existing skin disorders may be more susceptible to the effects of isoamyl acetate. Although isoamyl acetate is not known as a kidney toxin in humans, the importance of this organ in the elimination of toxic substances justifies special consideration in those with possible impairment of renal function. Although isoamyl acetate is not known as a liver toxin in humans, the importance of this organ in the biotransformation and detoxification of foreign substances should be considered before exposing persons with impaired liver function.

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**Substance** **Hepatotoxic**  
**Isobutyl Acetate** **N**

1. NIOSH Target Organs: Skin, eyes, respiratory system, central nervous system.
2. HSDB Medical Surveillance: Consider initial effects on skin and resp tract in any preplacement or periodical exam, as well as liver and kidney function.
3. HSDB Populations at Special Risk: Employees with skin, kidney, chronic respiratory, or liver disease may be at increased risk from isobutyl acetate exposure.

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**Substance** **Hepatotoxic**  
**Isobutyl Alcohol** **N**

1. IRIS Critical Effects: Hypoactivity and ataxia. Rat Oral Subchronic Study - U.S. EPA 1986
2. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
3. HSDB Medical Surveillance: An employee who is exposed to isobutyl alcohol at potentially hazardous levels should be screened for history of certain medical conditions skin, liver, kidney, eye, chronic respiratory, central and peripheral nervous system diseases which might place the employee at increased risk from isobutyl alcohol exposure. Any employee developing the conditions should be referred for further medical exam.
4. HSDB Populations at Special Risk: Individuals with liver, kidney, eye, or chronic respiratory diseases may be at increased risk.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Isopropyl Acetate</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
2. HSDB Populations at Special Risk: Employees with chronic respiratory, skin, **liver**, or kidney diseases may be at increased risk from isopropyl acetate.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Isopropyl Amine</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Lindane (Pesticide)*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, **liver**, kidneys.
2. HSDB Medical Surveillance: A complete history and physical examination: The purpose is to detect preexisting conditions that might place the exposed employee at an increased risk from exposure. Examination of the eyes, central nervous system, blood, **liver**, and kidneys should be stressed. The skin should be examined for evidence of chronic disorders. Lindane may cause aplastic anemia; A complete blood count should be performed, including a red cell count, a white cell count, and a differential count of a stained smear, as well as a hemoglobin and hematocrit. The concentration of lindane in the blood is an indication of the extent of absorption. Medical examinations should be repeated on an annual basis.
3. HSDB Populations at Special Risk: Lindane should not be used to treat pregnant woman, small infants or individuals with extensively excoriated skin. Preclude from exposure individuals with **liver**, or kidney diseases. Formulators, distributors and agricultural workers.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Malathion (Pesticide)*</b>	<b>Y</b>

1. IRIS Critical Effects: Red blood cell ChE depression. Subchronic Human Feeding Study - Moeller and Rider 1962.
2. NIOSH Target Organs: Eyes, skin, respiratory system, **liver**, blood cholinesterase, central nervous system, cardiovascular system, gastrointestinal tract.
3. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) evidence in humans: no adequate data; 2) evidence in animals: inadequate; Overall summary evaluation of carcinogenic risk to humans is group 3: The agent is not classifiable as to its carcinogenicity to humans.
4. HSDB Medical Surveillance: Placement & periodic medical examinations shall include: (a) Comprehensive initial or interim medical & work histories. (b) A physical exam which shall be directed toward, but not limited to evidence of frequent headache, dizziness, nausea, tightness of the chest, dimness of vision, & difficulty in focusing the eyes. (d) A judgment of the worker's physical ability to use negative or positive pressure regulators as defined in 29 CFR 1910.134. Examination of the respiratory system, **liver**, and attention to the cholinesterase levels in the blood should be stressed. Malathion can cause depressed levels of activity of cholinesterase in the serum and erythrocytes. The cholinesterase activity in the erythrocytes should be measured before employment (or exposure) in order to establish an individual baseline value, which should be the mean of two cholinesterase activity measurements, taken at least one day apart. The aforementioned medical examinations should be repeated on an annual basis,

with the exception of the cholinesterase determination which should be performed quarterly or at any time overexposure is suspected or signs and symptoms of toxicity occur. Medical records shall be maintained for all workers engaged in the manufacture or formulation of malathion and such records shall be kept for at least 1 year after termination of employment.

5. HSDB Populations at Special Risk: Persons with a history of reduced pulmonary function or recent exposure to anticholinesterase agents would be expected to be at increased risk from exposure.

Substance	Hepatotoxic
<b>Methoxychlor (Insecticide)*</b>	<b>Y</b>
1. IRIS Critical Effects: Excessive loss of litters. Rabbit Teratology Study - Kincaid Enterprise 1986.	
2. NIOSH Target Organs: Central nervous system, liver, kidneys ( <i>in animals; liver, and ovarian cancer</i> ).	
3. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) evidence in humans: no data; 2) evidence in animals: insufficient. Overall summary evaluation of carcinogenic risk to humans is Group 3: The agent is not classifiable as to its carcinogenicity to humans.	
4. HSDB Populations at Special Risk: 1. Women may be at increased risk along with individuals who have liver, kidney diseases, or convulsive disorders.	
5. Casarett and Doull: Methoxychlor is a member of the same pesticide family as DDT. Exposures to moderate or high non-fatal doses of DDT may result in pathologic changes withing the liver. Morphologic changes within the liver as a response to DDT exposure include hypertrophy of hepatocytes and subcellular organelles. High concentrations of DDT may produce centrilobular necrosis within the liver. (Casarett and Doull's Toxicology: The Basic Science of Poisons, Eds. Mary O. Amdur, John Doull, Curtis Klaasen, 4th edition, 1991.)	

Substance	Hepatotoxic
<b>Methyl Acrylate</b>	<b>N</b>
1. NIOSH Target Organs: Eyes, skin, respiratory system.	
2. HSDB Medical Surveillance: Employees should be screened for history of certain medical conditions (chronic respiratory disease, skin disease, liver disease & kidney disease) which might place the employee at increased risk from methyl acrylate exposure.	
3. HSDB Populations at Special Risk: certain medical conditions chronic respiratory disease, skin disease, liver disease & kidney disease might place the employee at increased risk from methyl acrylate exposure.	

Substance	Hepatotoxic
<b>Methyl Cellosolve (EMGME)</b>	<b>N</b>
1. IRIS Critical Effects: Testicular effects. Subchronic Inhalation Studies in Male New Zealand White Rabbits and Sprague-Dawley Rats - Miller et al., 1983.	
2. NIOSH Target Organs: Eyes, respiratory system, central nervous system, blood, kidneys, reproductive system, hematopoietic system.	

3. HSDB Medical Surveillance: Initial medical exam: Exam of the CNS should be stressed. A complete blood count should be performed including a red cell count, a white cell count, a differential count of a stained smear hemoglobin and hematocrit. Urinalysis. Periodic medical exam: The aforementioned medical exam should be repeated on an annual basis.

4. HSDB Populations at Special Risk: Individuals who are occupationally exposed to methyl cellosolve and have hematologic and or kidney disorders may be at increased risk.

Substance	Hepatotoxic
<b>Methyl Cellosolve Acetate</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, respiratory system, kidneys, brain, central nervous system, peripheral nervous system, reproductive system, hematopoietic system.

2. HSDB Medical Surveillance: SRP: Medical surveillance should emphasize monitoring of central nervous system, kidney and hematology in employees.

Substance	Hepatotoxic
<b>Methyl Chloride (Monochloromethane)*</b>	<b>Y</b>

1. NIOSH Target Organs: Central nervous system, liver, kidneys, reproductive system (*in animals; lung, kidney and forestomach tumors*).

2. HSDB Toxic Hazard Rating: The Human Health Assessment Group in EPA's Office of Health and Environmental Assessment has evaluated methyl chloride for carcinogenicity. According to their analysis, the weight-of-evidence for methyl chloride is group C, which is based on limited evidence in animals. No data are available for humans. As a group C chemical, methyl chloride is considered possibly carcinogenic to humans.

3. HSDB Medical Surveillance: Protect from exposure those individual with diseases of kidneys, liver, and CNS. Physical exam of exposed personnel every 6 months include studies of liver and kidney function.

4. HSDB Populations at Special Risk: Persons suffering from disorders of central nervous system, anemia, alcoholism or liver or kidney disease should be protected from working with chloromethane.

Substance	Hepatotoxic
<b>Methyl Chloroform (1,1,1-Trichloroethane)*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, central nervous system, cardiovascular system, liver.

2. HSDB Toxic Hazard Rating: No data are available in humans. Inadequate evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans. EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: There are no reported human data and animal studies (one lifetime gavage, one intermediate-term inhalation) have not demonstrated carcinogenicity. Technical grade 1,1,1-trichloroethane has been shown to be weakly mutagenic although the contaminant, 1,4-dioxane, a known animal carcinogen, may be responsible for this response. Human carcinogenicity data: None. ANIMAL CARCINOGENICITY DATA: Inadequate.

3. HSDB Medical Surveillance: To determine whether unchanged solvent urinary concentration could be used as a biological exposure index, workers occupationally exposed to various solvents were studied. Nine unrelated groups working in plastic boat, chemical, plastic button, paint, and shoe factories were

studied. A total of 659 males were monitored. Urine samples were collected at the beginning of the workshift and at the end of the first half of the shift. A close relationship (correlation coefficient always above 0.85) between the average environmental solvent concentration (mg/cu m) measured in the breathing zone and the urinary concentration of unchanged solvent (ug/l) was observed. The proposed Biological Equivalent Exposure Limit (805 ug/l) corresponded to the environmental Threshold Limit Value (860 ug/l) for 1,1,1-trichloroethane. Biological exposure data for urine collected over 4 hr during random sampling for at least 1 yr could be used to evaluate long-term exposure and probability of non-compliance for individual or groups of workers.

- HSDB Population at Special Risk: Individuals with diseases of the liver or kidneys would be at risk from exposure to 1,1,1-trichloroethane.

Substance	Hepatotoxic (Y in animals)
<b>Methylene Chloride (Dichloromethane)*</b>	
1. IRIS Critical Effects: Liver toxicity. 2-Year Rat Drinking Water Bioassay - National Coffee Association, 1982 (male and females respectively).	
2. NIOSH Target Organs: Eyes, skin, cardiovascular system, central nervous system ( <i>in animals; lung, liver, salivary and mammary gland tumors</i> ).	
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: B2; probable human carcinogen. BASIS FOR CLASSIFICATION: Based on inadequate human data and sufficient evidence of carcinogenicity in animals; increased incidence of hepatocellular neoplasms and alveolar bronchiolar neoplasms in male and female mice, and increased incidence of benign mammary tumors in both sexes of rats, salivary gland sarcomas in male rats and leukemia in female rats. This classification is supported by some positive genotoxicity data, although results in mammalian systems are generally negative. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient. Inadequate evidence of carcinogenicity in humans. sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans. A2. A2= Suspected human carcinogen.	
4. HSDB Medical Surveillance: The following medical procedures should be made available to each employee who is exposed to methylene chloride at potentially hazardous levels: Initial Medical Exam: The purpose is to detect existing conditions that might place employee at increased risk, & to establish baseline for future health monitoring. Exam of skin, liver, kidneys, CNS, & blood should be stressed. Clinical impressions of autonomic nervous system & pulmonary function made, with additional tests conducted where indicated. Skin disease: Methylene chloride can cause dermatitis on prolonged exposure. Persons with existing skin disorders may be more susceptible to effects of this agent. Liver disease: A profile of liver function should be obtained by utilizing medically acceptable array of biochemical tests. Kidney disease: Justifies special consideration before exposing persons with impaired renal function. Cardiovascular disease: Because of reports of excessive carbon monoxide levels following exposure persons with cardiac disease may be at increased risk. A complete blood count should be performed Carboxyhemoglobin values should be determined periodically, & level above 5% should prompt investigation of worker & his workplace. 2. Periodic medical exam: The aforementioned medical exam should be repeated on an annual basis. Persons should be cautioned against smoking due to smoke induced increase in carboxyhemoglobin levels in blood. Dichloromethane exposure in workers may be monitored by analysis of dichloromethane in blood or breath, or carbon monoxide in blood. Blood dichloromethane concern measured during exposure probably should not exceed 1 mg/l in subjects exposed at 100 ppm level for 8 hr. Breath dichloromethane concern averaged about 33 ppm during exposure to air containing 100 ppm of chemical. Blood & breath concern plateau after 2 hr of exposure, & decline rapidly after cessation of exposure. It should be noted that physical exertion during exposure can dramatically increased blood & breath content of dichloromethane. Pre-exposure specimens should be	

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

analyzed to establish background carboxyhemoglobin levels for each individual. PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.

5. HSDB Populations at Special Risk: The quantity of dichloromethane (DCM) absorbed is dependent on body weight and fat content of the body. The risk of accumulation of DCM in adipose tissue is expected to be greater for obese persons. Artists with cardiovascular impairment should not use materials containing methylene chloride.

Substance	Hepatotoxic
<b>Methyl Methacrylate</b>	<b>N</b>
1. NIOSH Target Organs: Eyes, skin, respiratory system.	
2. HSDB Toxic Hazard Rating: Evaluation: There is inadequate evidence in humans for the carcinogenicity of methyl methacrylate. There is evidence suggesting lack of carcinogenicity of methyl methacrylate in experimental animals. Overall evaluation: Methyl methacrylate is not classifiable as to its carcinogenicity to humans (Group3).	
3. HSDB Medical Surveillance: Employees should be screened for history of certain medical conditions (chronic resp, skin, kidney, & <b>liver</b> diseases) which might place the employee at increased risk from methyl methacrylate exposure.	
4. HSDB Populations at Special Risk: Certain medical conditions (chronic resp, skin, kidney, & <b>liver</b> diseases) might place the employee at increased risk from methyl methacrylate exposure.	

Substance	Hepatotoxic
<b>Mineral Oil</b>	<b>N</b>
1. No information found in IRIS and NIOSH Pocket Guide to Chemical Hazards.	
2. HSDB Populations at Special Risk: Oral mineral oil should not be given to patients with swallowing abnormalities. Oral administration of mineral oil is contraindicated in children younger than 6 years of age; in bedridden, geriatric, debilitated, or pregnant patients; and in patients with esophageal or gastric retention, dysphasia, or hiatal hernia.	

Substance	Hepatotoxic
<b>Naphtha (Coal Tar)*</b>	<b>Y</b>
1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, <b>liver</b> , kidneys.	
2. Medical Surveillance: Persons with history of skin diseases or who have predisposition to dust allergies should be excluded from work with tar. Worker should receive a periodic medical exam every 6 mo.	
3. In pigs coal tar poisoning causes <b>liver</b> hemorrhage and necrosis that is scattered and centrilobular. The liver looks mottled. Tissues are icteric. The <b>liver</b> is engorged and friable.	

Substance	Hepatotoxic
<b>p-Nitroaniline*</b>	<b>Y</b>
1. NIOSH Target Organs: Respiratory system, blood, heart, <b>liver</b> .	

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

2. HSDB Medical Surveillance: Consider the points of attack (blood, heart, lungs and liver) in preplacement and periodic physical examinations. Routine checking of lips, tongue and nail beds of exposed personnel for signs of cyanosis. Protect from exposure those individuals with anemia, cardiovascular or pulmonary diseases.

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Substance	Hepatotoxic Y
<b>Nitrobenzene*</b>	Y

1. IRIS Critical Effects: Hematologic, adrenal, renal, and hepatic lesions (*mice*) converted to Rat/Mouse Subchronic Inhalation Study - CIIT, 1984.
2. NIOSH Target Organs: Eyes, skin, blood, liver, kidneys, cardiovascular system, reproductive system.
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: Based on no data concerning carcinogenicity in humans or animals. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: None.
4. HSDB Medical Surveillance: Employment & periodic examinations should be concerned particularly in those with a history of blood dyscrasias, reactions to medications, alcohol intake, eye disease, skin, & cardiovascular status. Liver & renal functions should be evaluated periodically, as well as blood & general health. Follow methemoglobin levels until normal in all cases of suspected cyanosis. The metabolites in urine, p-nitro- & p-aminophenol, can be used as evidence of exposure.
5. HSDB Populations at Special Risk: Pregnant women may be especially at risk due to transplacental passage. Individuals with glucose-6-phosphate dehydrogenase deficiency may also be special risk groups. Additionally, because alcohol ingestion or chronic alcoholism can lower the lethal toxic dose of nitrobenzene, individuals consuming alcoholic beverages may be at risk. Persons with a history of blood dyscrasias, reactions to medications, or those with eye, skin, and cardiovascular disease.

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Substance	Hepatotoxic Y
<b>Paraquat (Pesticide)*</b>	Y

1. IRIS Critical Effects: Chronic pneumonitis. 1-Year Dog Feeding Study - Chevron Chemical Company, 1983a.
2. NIOSH Target Organs: Eyes, skin, respiratory system, heart, liver, kidneys, gastrointestinal tract.
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: C; possible human carcinogen. Basis for Classification: Paraquat produced squamous cell carcinoma, an uncommon tumor, in the head region in both sexes of Fischer 344 rats. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Limited.
4. HSDB Medical Surveillance: Recommended medical surveillance: Initial medical examinations: A complete history and physical examination is recommended. Examination of the eyes, respiratory system, heart, liver, and kidneys should be stressed. The skin should be examined for evidence of chronic disorders. A 14 in x 17 in chest roentgenogram, FVC and FEV (1 sec), urinalysis specific gravity, albumin, glucose, and a microscopic on centrifuged sediment, and liver function tests should be performed. The aforementioned medical examinations should be repeated on an annual basis.
5. HSDB Populations at Special Risk: Persons with impaired pulmonary function may be at increased risk from exposure.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Parathion (Pesticide)</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, cardiovascular system, blood cholinesterase.
2. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) evidence in humans: no adequate data; 2) evidence in animals: limited. Overall summary evaluation of carcinogenic risk to humans is Group 3: The agent is not classifiable as to its carcinogenicity to humans. EPA CLASSIFICATION: C; possible human carcinogen. Basis for Classification: Increased adrenal cortical tumors in female and male Osborne-Mendel rats and positive trends for thyroid follicular adenomas and pancreatic islet-cell carcinomas in male rats in one study. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Limited.
3. HSDB Medical Surveillance: All workers exposed to parathion should be under medical supervision. At employment exam the doctor should obtain occupational and medical information pertinent to protecting the employee from parathion. Before worker has been exposed blood levels of both red cell and plasma cholinesterase determined to establish baseline. These tests should be repeated at regular intervals, depending on degree of exposure. A physical examination which shall be directed towards, but not limited to, evidence of frequent headaches, dizziness, nausea, tightness of the chest, dimness of vision, and difficulty in focusing the eyes. Those workers with a history of glaucoma, cardiovascular disease, hepatic disease, renal disease, or central nervous system abnormalities should be considered for exclusion from assignments requiring exposure to parathion. Medical records shall be maintained for all workers occupationally exposed to parathion and such records shall be kept for at least 5 years after termination of employment. A complete history and physical examination to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring should be done. Persons with a history of reduced pulmonary function, convulsive disorders, or recent exposure to anticholinesterase agents would be expected to be at increased risk from exposure. Examination of the respiratory system, nervous system, cardiovascular system, eyes, and attention to cholinesterase levels in the blood should be stressed. The skin should be examined for evidence of chronic disorders. Cholinesterase determination: Parathion causes depressed levels of activity of cholinesterase in the serum and erythrocytes. The cholinesterase activity in the serum and erythrocytes should be determined by using medically acceptable biochemical tests prior to any new period of exposure. The aforementioned medical examination should be repeated on an annual basis, with exception of the cholinesterase determination. This test should be performed at four week intervals, except for those employees in areas which may involve intense exposure, for whom the test should be repeated weekly. If any employee works more than 12 hr/day, they should be tested every three weeks. Employees should be also tested at any time over exposure is suspected or signs or symptomology of toxicity appear. Any employee having a 30-40% decreased in cholinesterase should be removed from exposure and placed under medical observation.
4. HSDB Populations at Special Risk: Workers with history of glaucoma, cardiovascular, hepatic, or renal diseases, or CNS abnormalities should be considered for assignments involving non-exposure to parathion. Persons with a history of reduced pulmonary function, convulsive disorders, or recent exposure to anticholinesterase agents would be expected to be at increased risk from exposure.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Pentaborane</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, central nervous system.
2. HSDB Medical Surveillance: Employment and periodic physical examinations should be performed. These examinations should be concerned with any history of central nervous system disease, personality, or behavioral changes, as well as liver, kidney, or pulmonary disease of any significant nature. Protect

from exposure those individuals with history of blood disorders, allergies, and diseases of the lung, kidneys, and liver.

Substance	Hepatotoxic
<b>Pentachloronaphthalene (Halowax 1013)*</b>	<b>Y</b>

1. NIOSH Target Organs: Skin, liver, central nervous system.

Substance	Hepatotoxic
<b>Pentachlorophenol (fungicide)*</b>	<b>Y</b>

1. IRIS Critical Effects: Liver and kidney pathology. Rat Oral Chronic Study - Schwetz et al., 1978.
2. NIOSH Target Organs: Eyes, skin, respiratory system, cardiovascular system, liver, kidneys, central nervous system.
3. HSDB Toxic Hazard Rating: Evaluation: There is inadequate evidence in humans for the carcinogenicity of pentachlorophenol. There is sufficient evidence in experimental animals for the carcinogenicity of pentachlorophenol. Overall evaluation: Pentachlorophenol is possibly carcinogenic to humans (2B). EPA CLASSIFICATION: B2; probable human carcinogen Basis for Classification: The classification is based on inadequate human data and sufficient evidence of carcinogenicity in animals: statistically significant increases in the incidences of multiple biologically significant tumor types (hepatocellular adenomas and carcinomas, adrenal medulla pheochromocytomas, and malignant pheochromocytomas, and/or hemangiomas) in one or both sexes of B6C3F1 mice using two different preparations of pentachlorophenol. In addition, a high incidence of two uncommon tumors (adrenal medulla pheochromocytomas and hemangiomas/hemangiosarcomas) was observed with both preparations. The classification is supported by mutagenicity data, which provides some indication that pentachlorophenol has clastogenic potential. HUMAN CARCINOGENICITY DATA: Inadequate. ANIMAL CARCINOGENICITY DATA: Sufficient.
4. HSDB Medical Surveillance: A complete history and physical examination initially, followed by annual complete physical examinations.
5. HSDB Populations at Special Risk: Individuals suffering from kidney and liver diseases should be protected from occupational exposure.

Substance	Hepatotoxic
<b>n-Pentane</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
2. HSDB Medical Surveillance: Consider the points of attack skin, eyes, respiratory system, lung in preplacement and periodic physical examinations.
3. HSDB Populations at Special Risk: Persons with skin disorders may be more susceptible to the effects of this agent. In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of pentane might cause exacerbation of symptoms due to its irritant properties.

Substance	Hepatotoxic
<b>2-Pentanone</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Petroleum Distillates (Naphtha)</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Phenol*</b>	<b>Y</b>

1. IRIS Critical Effects: Reduced fetal body weight in rats. Rat Oral Developmental Study - NTP 1983.
2. NIOSH Target Organs: Eyes, skin, respiratory system, **liver**, kidneys.
3. HSDB Medical Surveillance: There is some suggestive evidence that a biologic monitoring method may be useful for detecting an excessive internal dose on an individual and or on a group basis for phenol. Tentative max value in urine <20 mg/g creatinine, permissible value 300 mg/g creatinine. From table Physical examinations of exposed personnel annually, including studies of **liver** and kidney function. Protect those individuals with diseases of central nervous system, **liver**, kidney, and lung.
4. HSDB Populations at Special Risk: Those affected with hepatic or kidney diseases should not be exposed to phenol for any length of time, because even intermittent exposure to vapors may become dangerous, particularly when handled at elevated temp.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Phenyl Ether Vapor (Phenoxybenzene)</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Phenyl Hydrazine*</b>	<b>Y</b>

1. NIOSH Target Organs: Blood, respiratory system, **liver**, kidneys, skin (*in animals; tumors of the lungs, liver, blood vessels and intestine*).
2. HSDB Medical Surveillance: Situations in which air concern approaches 5 ppm and particularly where there is additional possibility of skin contact, workers should be under careful medical observation. It is essential that alcoholics or persons suffering from **liver** ailments or blood disorders are protected from work with phenylhydrazine. Complete periodic medical exams should include blood tests, as well as biochemical tests (glycemia, cholesterolemia, bilirubinemia). Urine should be examined for degradation products of phenylhydrazine.
3. HSDB Populations at Special Risk: Individuals with G6PD glucose-6-phosphate dehydrogenase deficiency have been found to be more susceptible to hemolytic effects of phenylhydrazine than those who do not have a deficiency.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Phosgene</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system.
2. HSDB Medical Surveillance: Pre-employment medical examinations should include chest X-rays and baseline pulmonary function tests. The eyes and skin should be examined and the smoking history should be known. Periodic pulmonary function studies should be done. Workers who are known to have inhaled

phosgene should remain under medical observation for at least 24 hours to insure that delayed symptoms do not occur.

Substance	Hepatotoxic
<b>Phosphine (Pesticide)</b>	N

1. IRIS Critical Effects: Body weight and clinical parameters. Rat Chronic Oral Study - Hackenburg 1972.
2. NIOSH Target Organs: Respiratory system.
3. HSDB Toxic Hazard Rating: EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: Based on inadequate data in animals and no tumor data in humans. While phosphine has not been associated with cancer in humans, there is some evidence of chromosomal damage (transient chromatic deletions, gaps and breaks, persistent chromosomal translocations). A relationship between these genetic effects and the development of cancer in humans is sometimes postulated. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Inadequate.

Substance	Hepatotoxic
<b>n-Propyl Acetate</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
2. HSDB Populations at Special Risk: Employees with chronic respiratory, skin, kidney, or liver disease may be at increase risk.

Substance	Hepatotoxic
<b>n-Propyl Alcohol</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system, gastrointestinal tract, central nervous system.
2. HSDB Medical Surveillance: The following medical procedures should be made available to each employee who is exposed to propyl alcohol at potentially hazardous levels: 1. Initial medical screening: Employees should be screened for history of certain medical conditions (listed below) which might place the employee at increased risk from propyl alcohol exposure. Skin disease: Propyl alcohol is a defatting agent and can cause dermatitis on prolonged exposure. Persons with preexisting skin disorders may be more susceptible to the effects of this agent. Liver disease: Although propyl alcohol is not known as a liver toxin in humans, the importance of this organ in the biotransformation and detoxification of foreign substances should be considered before exposing persons with impaired liver function. Kidney disease: Although propyl alcohol is not known as a kidney toxin in humans, the importance of this organ in the elimination of toxic substances justifies special consideration in those with impaired renal function. Chronic respiratory disease: In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of propyl alcohol might cause exacerbation of symptoms due to its irritant properties. Periodic Medical Examination: Any employee developing the above listed conditions should be referred for further medical examinations.
3. HSDB Populations at Special Risk: Persons with preexisting skin disorders may be more susceptible to the effects of this agent. In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of propyl alcohol might cause exacerbation of symptoms due to its irritant properties.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Propylene Dichloride (Pesticide)*</b>	<b>Y</b>

1. IRIS Critical Effects: Hyperplasia of the nasal mucosa. Rat 13-Week Inhalation Study - Nitschke et al., 1988.
2. NIOSH Target Organs: Eyes, skin, respiratory system, **liver**, kidneys, central nervous system (*in animals; liver and mammary gland tumors*).
3. HSDB Medical Surveillance: Recommended medical surveillance: 1) Initial medical screening: Employees should be screened for history of certain medical conditions which might place employee at increased risk such as skin disease, **liver** disease, kidney disease, & chronic resp disease 2) Periodic medical exam: Any employee developing the above-listed conditions should be referred for further medical exam. Evaluate the skin, **liver**, and renal function on a periodic basis, as well as cardiac and respiratory status & general health.
4. HSDB Populations at Special Risk: Persons with existing skin disorders may be more susceptible to the effects of this agent as well as persons with impaired **liver** function. Special consideration should be given before exposing persons with impaired renal function. In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of propylene dichloride might cause exacerbation of symptoms due to its irritant properties.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Pyrethrum</b>	<b>N</b>

1. NIOSH Target Organs: Respiratory system, skin, central nervous system.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Pyridine*</b>	<b>Y</b>

1. IRIS Critical Effects: Increased **liver** weight. 90-Day Rat Oral Study - U.S. EPA 1986.
2. NIOSH Target Organs: Eyes, skin, central nervous system, **liver**, kidneys, gastrointestinal tract.
3. HSDB Medical Surveillance: The following medical procedures should be made available to each employee who is exposed to pyridine at potentially hazardous levels: 1. Initial Medical Examination: A complete history and physical examination to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Examination of the central nervous system, **liver**, and kidneys should be stressed. The skin should be examined for evidence of chronic disorders. Urinalysis: Kidney damage has been reported from oral administration of pyridine to humans for therapeutic purposes. A urinalysis should be performed, including at a minimum specific gravity, albumin, glucose, and a microscopic examination on centrifuged sediment. **Liver** function tests: Pyridine may cause **liver** damage. A profile of **liver** function should be performed by using a medically acceptable array of biochemical tests. 2. Periodic Medical Examination: to be repeated on an annual basis.
4. HSDB Populations at Special Risk: Employees with existing central nervous system, **liver**, or kidney diseases are at increased risk.

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Stoddard Solvent (Mineral Spirits)</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, kidneys.

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Strychnine (Pesticide)</b>	<b>N</b>

1. IRIS Critical Effects: Toxicity/histopathology. Rat Oral Short-term to Subchronic Study - Seidl and Zbinden 1982.
2. NIOSH Target Organs: Central nervous system.
3. HSDB Medical Surveillance: Initial Medical Screening: Employees should be screened for history of certain medical conditions which might place the employee at increased risk from strychnine exposure. Persons with a history of convulsive disorders may be more susceptible to the effects of this agent. 2) Periodic Medical Examination: Any employee developing convulsive disorders should be referred for further medical examination.
4. HSDB Populations at Special Risk: Persons with a history of convulsive disorders may be more susceptible to the effects of this agent.

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<b>Substance</b>	<b>Hepatotoxic</b>
<b>Sulfur Dioxide</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system.
2. HSDB Toxic Hazard Rating: Evaluation: There is inadequate evidence for the carcinogenicity in humans of sulfur dioxide, sulfites, bisulfites and metabisulfites. There is limited evidence for the carcinogenicity in experimental animals of sulfur dioxide. There is inadequate evidence for the carcinogenicity in experimental animals of sulfites, bisulfites and metabisulfites. Overall evaluation: Sulfur dioxide, sulfites, bisulfites and metabisulfites are not classifiable as to their carcinogenicity to humans (Group 3).
3. HSDB Medical Surveillance: Preplacement and annual medical examinations should be done whenever TWA exposures exceed 0.25 ppm (0.65 mg/cu m). These examinations should be directed toward complaints of mucous membrane irritation, cough and shortness of breath. They should ascertain that nasal passages are open. Persons with a history of asthma or with subnormal pulmonary function should be watched closely. Simple expiatory function tests should be a part of the examination. They are useful for several purposes: (a) determining whether or not a person is a suitable candidate for using respirators; (b) identifying "reactors", i.e., persons who may be most susceptible to the effects of SO<sub>2</sub>. This can be done by comparing preshift and postshift tests; (c) when done periodically, they can be used to determine whether or not a person's expiatory functions are declining at a faster than normal rate. Such determinations are much more sensitive when pooled data from a number of individuals are used. The forced expiatory volume at 1 second and the maximum mid-expiatory flow rate appear to be the most useful of the simple pulmonary function tests. Persons to be employed on work where there may be exposure to sulfur dioxide should receive preemployment medical examinations: persons suffering from chronic conjunctivitis or laryngitis, bronchitis, emphysema, bronchial asthma, any disorder inhibiting nasal resp, or any cardiovascular disease must be adequately exposed to this substance.
4. HSDB Populations at Special Risk: Persons with a history of asthma or with subnormal pulmonary function should be watched closely . Clear cut evidence has been obtained that asthmatic individuals are especially sensitive to sulfur dioxide. The degree of sensitivity to Sulfur dioxide appears to depend on the magnitude of preexisting airway hypersensitivity. Persons suffering from any cardiovascular disease should be adequately protected to this substance. In high-exposure communities (community mean specific sulfur dioxide level of 45 ug/cu m over 5 yr), smokers and nonsmokers had a higher incidence of persistent cough and sputum production compared with controls in low-exposure communities. Smoking remained the most important variable of the prevalence of persistent cough and sputum production.

Persons suffering from chronic conjunctivitis or laryngitis, bronchitis, emphysema, bronchial asthma, any disorder inhibiting nasal resp, or any cardiovascular disease should not be exposed to this substance.

Substance	Hepatotoxic
<b>Sulfur Pentafluoride</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.

Substance	Hepatotoxic
<b>Sulfuryl Fluoride</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, kidneys.
2. HSDB Medical Surveillance: Consider the points of attack (respiratory system, central nervous system) in preplacement and periodic physical examination.

Substance	Hepatotoxic
<b>1,1,2,2-Tetrachloro-1,2-Difluoroethane (freon 112)</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system.
2. HSDB Populations at Special Risk: It is possible that patients with cardiovascular or respiratory disorders may prove especially susceptible to aerosol propellants. In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of 1,1,2,2-tetrachloro-1,2-dichloroethane might cause exacerbation of symptoms due to its irritant properties.

Substance	Hepatotoxic
<b>1,1,2,2-Tetrachloroethane*</b>	Y

1. NIOSH Target Organs: Skin, liver, kidneys, central nervous system, gastrointestinal tract (*in animals; liver tumors*).
2. HSDB Toxic Hazard Rating: Inadequate evidence of carcinogenicity in humans. Limited evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans. EPA CLASSIFICATION: C; possible human carcinogen. Basis for Classification: Increased incidence of hepatocellular carcinomas in mice. HUMAN CARCINOGENICITY DATA: None.
3. HSDB Medical Surveillance: Preplacement medical exam should include at least: 1) Comprehensive medical and work histories with special emphasis directed to symptoms related to the liver, kidneys, and nervous system. Information about exposure to other chemicals should be recorded, as should episodes of nausea, vomiting, dizziness or headaches; 2) A physical exam; 3) Liver function tests, such as serum transaminase determinations, shall be performed, and screening tests of nervous system function should be considered by the responsible physician; 4) Judgment of the worker's ability to use positive or negative pressure respirators.
4. HSDB Populations at Special Risk: Workers with a tendency to liver disease, especially habitual drinkers of alcoholic beverages, and obese individuals also appear abnormally susceptible to tetrachloroethane.

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

<b>Substance</b>	<b>Hepatotoxic</b>
<b>Tetrachloroethylene (Perchloroethylene)*</b>	<b>Y</b>

1. IRIS Critical Effects: Hepatotoxicity in mice, weight gain in rats. 6-Week Mouse Gavage Study - Buben and O'Flaherty 1985.
2. NIOSH Target Organs: Eyes, skin, respiratory system, **liver**, kidneys, central nervous system (*in animals; liver tumors*).
3. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) Evidence in humans: inadequate; 2) evidence in animals: sufficient; Overall summary evaluation of carcinogenic risk to humans is group 2B: The agent is possibly carcinogenic to humans. A3. A3= Animal carcinogen.
4. HSDB Medical Surveillance: Periodical exam of the **liver** and kidneys. Exhaled air was analyzed for tetrachloroethene in teachers and 4-5 year old pupils of a kindergarten situated near a factory, and in residents of an old folks home situated near a former chemical waste dump. The tetrachloroethene concentrations were higher in the exhaled air of children living near the factory (mean 24 ug/cu m, n= 6) than in control children (mean 2.8 ug/cu m, n= 11). In the old folks home, the tetrachloroethene concentrations in the exhaled air of people living on the first floor were higher (mean 7.8 ug/cu m, n= 10) than in the exhaled air of the people living on the second floor and higher (mean 1.8 ug/cu m, n= 19). From the results of this study, it is clear that in environmental exposure to tetrachloroethene, biological monitoring of exhaled air is a simple, efficient, effective, and convenient method of assessing total ambient exposure of both young and aged subjects. PRECAUTIONS FOR "CARCINOGENS": in relation specifically to cancer hazards, there are at present no health monitoring methods that may ensure the early detection of preneoplastic lesions or lesions which may precede them. Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning additional tests that might become useful or mandatory.
5. HSDB Populations at Special Risk: individuals with diseases of the heart, **liver**, kidneys, and lung.

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<b>Substance</b>	<b>Hepatotoxic</b>
<b>Tetrahydrofuran</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, respiratory system, central nervous system.
2. HSDB Medical Surveillance: Consider the points of attack eyes, skin, resp system, CNS in preplacement and periodic physical exam. The following medical procedures should be made available to each employee who is exposed to tetrahydrofuran at potentially hazardous levels: (1) Initial Medical Screening: Employees should be screened for history of certain medical conditions (listed below) which might place the employee at increased risk from tetrahydrofuran exposure. These are skin, **liver**, kidney, and chronic respiratory diseases. (2) Periodic Medical Examination: Any employee developing the above listed conditions should be referred for further medical examination.
3. HSDB Populations at Special Risk: Persons with existing skin disorders may be more susceptible to the effects of tetrahydrofuran exposure.

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<b>Substance</b>	<b>Hepatotoxic</b>
<b>Toluene*</b>	<b>Y</b>

1. IRIS Critical Effects: Changes in **liver** and kidney weights. 13-Week Rat Gavage Study - NTP 1989 Neurological effects. Occupational Study Degeneration of nasal epithelium. 2-Year Rat Chronic Inhalation Study - NTP 1990.

2. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, **liver**, kidneys.

3. HSDB Toxic Hazard Rating: Evaluation: There is inadequate evidence for the carcinogenicity of toluene in humans. There is inadequate evidence for the carcinogenicity of toluene in experimental animals. Overall evaluation: Toluene is not classifiable as to its carcinogenicity to humans. EPA CLASSIFICATION: D; not classifiable as to human carcinogenicity. Basis for Classification: No human data and inadequate animal data. Toluene did not produce positive results in the majority of genotoxic assays. HUMAN CARCINOGENICITY DATA: None.

4. HSDB Medical Surveillance: Yearly physical examinations of exposed personnel, with special attention to the eyes and central nervous system, including complete blood count and **liver** function tests. The clinical examination should include hemocytometric testing and a thrombocyte (platelet) count in view of the possibility that toluene may contain a certain proportion of benzene. Hippuric acid levels above 5 g/l of urine may result from exposure greater than 200 ppm determined as a time weighted average.

5. HSDB Populations at Special Risk: Preclude individuals from exposure to toluene who have central nervous system or **liver** diseases.

Substance	Hepatotoxic
<b>Toluene 2,4-Diisocyanate*</b>	<b>Y</b>
1. NIOSH Target Organs: Eyes, skin, respiratory system ( <i>in animals; pancreas, liver, mammary gland and skin tumors</i> ).	
2. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) evidence in humans: no data; 2) evidence in animals: sufficient. Overall summary evaluation of carcinogenic risk to humans is Group 2B; the agent is possibly carcinogenic to humans.	
3. HSDB Medical Surveillance: Complete biologic monitoring, including pulmonary function and immunologic studies, has been performed concurrently with comprehensive environmental monitoring program in plant manufacturing toluene 2,4-diisocyanate. Protect from exposure those individuals with diseases of blood and <b>liver</b> . Physical exam of exposed personnel annually, include blood count and <b>liver</b> functions. The following steps were recommended: The entire factory population should be surveyed periodically for symptoms of lower respiratory tract diseases and lung function abnormalities that may be caused by chemical exposure; toluene diisocyanate exposure should be ended for sensitized workers or for those with excessive decline in lung function. Precautions for "Carcinogens": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.	
4. HSDB Populations at Special Risk: In view of potentially hazardous levels of toluene diisocyanate in commercially available aerosols, products should be properly labeled and patient with allergic diatheses and obstructive lung disease cautioned against their use. Individuals once sensitized are vulnerable to serious health consequences. Individuals with diseases of the blood or <b>liver</b> may be at an increased risk from exposure to this chemical.	

Substance	Hepatotoxic
<b>o-Toluidine*</b>	<b>Y</b>
1. NIOSH Target Organs: Eyes, skin, blood, kidneys, <b>liver</b> , cardiovascular system ( <i>in animals; liver, bladder and mammary gland tumors</i> ).	

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

2. HSDB Toxic Hazard Rating: The Human Health Assessment Group in EPA's Office of Health and Environmental Assessment has evaluated o-toluidine for carcinogenicity. According to their analysis, the weight-of-evidence for o-toluidine is group B2, which is based on inadequate evidence in humans and sufficient evidence in animals. As a group B2 chemical, o-toluidine is considered probably carcinogenic to humans. A2, skin. A2= Suspected human carcinogen. Inadequate evidence of carcinogenicity in humans. Sufficient evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 2B: The agent is possibly carcinogenic to humans.

3. HSDB Medical Surveillance: PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory. Routine examination of lips, tongue, and nail beds for diagnosis of cyanosis.

Substance	Hepatotoxic
<b>Tributyl Phosphate</b>	N

1. NIOSH Target Organs: Eyes, skin, respiratory system.

2. HSDB Medical Surveillance: All persons handling these substances should have regular, careful medical examinations with particular reference to the occurrence of any effects on the central nervous system. Phosphate esters cholinesterase determinations may be helpful in some instances in establishing the fact that some absorption has occurred although there is little evidence at present that they will be helpful in establishing the extent of exposure nor in predicting the likelihood of toxic symptoms.

Substance	Hepatotoxic
<b>1,1,2-Trichloroethane*</b>	Y

1. IRIS Critical Effects: Clinical serum chemistry. Mouse Subchronic Drinking Water Study - White et al., 1985 - Sanders et al., 1985.

2. NIOSH Target Organs: Eyes, respiratory system, central nervous system, liver, kidneys (*in animals; liver cancer*).

3. HSDB Toxic Hazard Rating: No data are available in humans. Limited evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans. EPA CLASSIFICATION: C; possible human carcinogen. Basis for Classification: Hepatocellular carcinomas and pheochromocytomas in one strain of mice forms the basis for this classification. Carcinogenicity was not shown in rats. 1,1,2-Trichloroethane is structurally related to 1,2-Dichloroethane, a probable human carcinogen. HUMAN CARCINOGENICITY DATA: None.

4. HSDB Medical Surveillance: The diagnosis of exposure can be established by expired breath or blood analysis.

5. HSDB Populations at Special Risk: Those individuals who are exposed to known hepatotoxins or have liver disease may (also) constitute a group at risk.

Substance	Hepatotoxic
<b>Trichloroethylene*</b>	Y

1. NIOSH Target Organs: Eyes, skin, respiratory system, heart, liver, central nervous system (*in animals; liver and kidney cancer*).

2. HSDB Toxic Hazard Rating: Inadequate evidence of carcinogenicity in humans. Limited evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans.

3. HSDB Medical Surveillance: Preplacement and periodic exam should include the skin, resp, cardiac, central, and peripheral nervous systems, as well as liver and kidney function. Alcohol intake should be evaluated. Effective medical supervision requires an adequate assessment of the level of exposure. This should be achieved by environmental monitoring as well as by biological monitoring. Protect from exposure those individuals with diseases of central nervous system, lung, liver, and kidneys.

PRECAUTIONS FOR "CARCINOGENS": Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning cytogenetic and or other tests that might become useful or mandatory.

Substance	Hepatotoxic
<b>1,1,2-Trichloro-1,2,2-Trifluoroethane (Freon 113)</b>	N
1. IRIS Critical Effects: Psychomotor impairment. Epidemiologic Study - Human Occupational Exposure - Imbus and Adkins 1972.	
2. NIOSH Target Organs: Skin, heart, central nervous system, cardiovascular system.	
3. HSDB Medical Surveillance: Employees should be screened for history of certain medical conditions (listed below) which might place the employee at increased risk from exposure. 1,1,2-Trichloro-1,2,2-trifluoroethane is a defatting agent and can cause dermatitis on prolonged exposure. Persons with existing skin disorders may be more susceptible to the effects of this agent. In persons with impaired cardiovascular function, especially those with a history of cardiac arrhythmias, the breathing of 1,1,2-trichloro-1,2,2-trifluoroethane might cause exacerbation of symptoms due to its sensitizing properties. Any employee developing the above-listed conditions should be referred for further medical examination.	
4. HSDB Populations at Special Risk: Persons with existing skin disorders may be more susceptible to the effects of this agent. In persons with impaired cardiovascular function, especially those with history of cardiac arrhythmias, the breathing of 1,1,2-trichloro-1,2,2-trifluoroethane might cause exacerbation of symptoms due to its sensitizing properties.	

Substance	Hepatotoxic
<b>Triethylamine*</b>	Y
1. IRIS Critical Effects: No observed adverse effects. 28-Week Rat Inhalation Study - Lynch et al., 1990 Inflammation of the nasal passage. 10-Day Rat Inhalation Study - Virginia Chemicals 1987.	
2. NIOSH Target Organs: Eyes, skin, respiratory system, cardiovascular system, liver, kidneys.	
3. HSDB Medical Surveillance: 1. Employee who will be exposed to triethylamine at potentially hazardous levels should be screened for history of certain medical conditions chronic respiratory diseases, cardiovascular diseases, liver diseases, kidney diseases, eye diseases which might place the employee at increased risk from triethylamine exposure. Any employee developing the conditions should be referred for further medical exam.	
4. Triethylamine has caused liver damage in rabbits at 100 ppm. OSHA's PEL is 25 ppm.	

\* Identified a Hepatotoxic in NIOSH Pocket Guide to Chemical Hazards, June 1994 Edition

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<b>Substance</b>	<b>Hepatotoxic</b>
<b>Trifluorobromomethane (Halon 1301)</b>	<b>N</b>

1. NIOSH Target Organs: Central nervous system, heart.
2. HSDB Medical Surveillance: Consider the points of heart attack, central nervous system in preplacement and periodic physical examinations. The following medical procedures should be made available to each employee who is exposed to trifluoromonobromomethane at potentially hazardous levels:  
Initial Medical Screening: Employees should be screened for history of certain medical conditions which might place the employee at increased risk from trifluoromonobromomethane exposure. These include cardiovascular disease: In persons with impaired cardiovascular function, especially those with a history of cardiac arrhythmias, the breathing of trifluoromonobromomethane might cause exacerbation of symptoms due to its sensitizing properties. 2. Periodic Medical Examination: Any employee developing these conditions should be referred for further medical examination.
3. HSDB Populations at Special Risk: In persons with impaired pulmonary function, especially those with obstructive airway diseases, the breathing of Refrigerant 114 might cause exacerbation of symptoms due to its irritant properties. In persons with impaired cardiovascular function, especially those with history of cardiac arrhythmias, the inhalation of Refrigerant 114 might cause exacerbation of disorders of the conduction mechanism due to sensitizing effects on the myocardium. It is possible that patient with cardiac or respiratory disorders may prove especially susceptible.

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<b>Substance</b>	<b>Hepatotoxic</b>
<b>Triorthocresylphosphate</b>	<b>N</b>

1. NIOSH Target Organs; Peripheral nervous system, central nervous system.
2. HSDB Medical Surveillance: Persons to be employed or work in which there is a danger of exposure to tricresyl phosphates should receive a pre-employment medical examination; persons with cardiorenal or nervous disorders should be protected.

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<b>Substance</b>	<b>Hepatotoxic</b>
<b>Triphenyl Phosphate</b>	<b>N</b>

1. NIOSH Target Organs: Blood, peripheral nervous system.
2. HSDB Medical Surveillance: Employees should be screened for history of neuromuscular disorders which might place the employee at great risk from triphenyl phosphate exposure.
3. HSDB Populations at Special Risk: Triphenyl phosphate causes neurotoxic effects in animals. Persons with preexisting neuromuscular disorders may be at increased risk.

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<b>Substance</b>	<b>Hepatotoxic</b>
<b>Turpentine</b>	<b>N</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, kidneys.
2. HSDB Medical Surveillance: Consideration should be given to skin disease or skin allergies in any preplacement or periodic examinations. Liver, renal, and respiratory diseases should also be considered.
3. HSDB Populations at Special Risk: Persons with preexisting skin disorders, liver disease, chronic respiratory disease, and kidney disease.

Substance	Hepatotoxic
<b>Vinyl Chloride*</b>	<b>Y</b>

1. NIOSH Target Organs: **Liver**, central nervous system, blood, respiratory system, lymphatic system (*liver cancer*).
2. HSDB Toxic Hazard Rating: Classification of carcinogenicity: 1) evidence in humans: sufficient; 2) evidence in animals: sufficient; Overall summary evaluation of carcinogenic risk to humans is group 1: The chemical is carcinogenic to humans. A1. A1= Confirmed human carcinogen.
3. HSDB Medical Surveillance Rating: Exam by wide field capillary microscopy of the hands of polyvinyl chloride workers demonstrated capillary abnormalities in a high percentage of exposed men. This non-invasive technique may be useful as a mass screening procedure in the early detection of vinyl chloride induced disease. A placement examination should include an employment history, and a personal history, which should also contain information about alcohol and cigarette consumption, previous episodes of hepatitis, exposures to hepatotoxic agents, and hospitalizations. It is also advisable to carry out a number of laboratory examinations and tests: chest radiography, ECG, blood count, determination of SGOT and SGPT, total bilirubin, alkaline phosphates, gamma-glutamyl transpeptidase, and urinalysis. Periodic medical examinations may be carried out every 12 months (or every 6 months for workers with particularly high exposure). PRECAUTIONS FOR "CARCINOGENS": In relation specifically to cancer hazards, there are at present no health monitoring methods that may ensure the early detection of preneoplastic lesions or lesions which may preclude them. Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning additional tests that might become useful or mandatory.
4. HSDB Populations at Special Risk: Older individuals, females, newborns, and alcohol consumers may be particularly sensitive to the effects of vinyl chloride. Those individuals with **liver**, renal, cardiac, or pulmonary impairments.

Substance	Hepatotoxic
<b>Xylenes (o-,m-,p- isomers)*</b>	<b>Y</b>

1. NIOSH Target Organs: Eyes, skin, respiratory system, central nervous system, gastrointestinal tract, blood, **liver**, kidneys.
2. HSDB Toxic Hazard Rating: Evaluation: There is inadequate evidence for the carcinogenicity of xylene in humans. There is inadequate evidence for the carcinogenicity of xylene in experimental animals. Overall evaluation: Xylene is not classifiable as to its carcinogenicity to humans.
3. HSDB Medical Surveillance: Physical examinations of exposed personnel annually, with special attention to eyes and central nervous system, and include complete blood count and studies of **liver** and kidney function.
4. HSDB Populations at Special Risk: Those individuals with diseases of the central nervous system, **liver**, kidneys, or blood.

Substance	Hepatotoxic
<b>Xylidine (o-,m-,p- isomers)*</b>	<b>Y</b>

1. NIOSH Target Organs: Respiratory system, blood, **liver**, kidneys, cardiovascular system.
2. HSDB Toxic Hazard Rating: A2, skin. A2= Suspected human carcinogen.

3. HSDB Medical Surveillance: Initial medical examination: A complete history & physical examination. The purpose is to detect existing conditions that might place the exposed employee at increased risk, and to establish a baseline for future health monitoring. Exam of the blood, lungs, liver, kidneys, and cardiovascular system should be stressed. Periodic medical exam should be repeated on an annual basis.

**REGULATORY VALUES**

CHEMICAL	ACGIH TLVs				OSHA PELs				NIOSH RELs				CARCINOGENICITY CLASSIFICATION	
	TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		IRIS	ACGIH
	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m		
Acetaldehyde					200	360							B2	A3
Acetic Acid	10	25	15	37	10	25			10	25	15	37		
Acetone	750	1780	1000	2380	1000	2400			250	590			D	
Acetonitrile	40	67	60	101	40	70			20	34				
Acrolein	0.1	0.23	0.03	0.69	0.1	0.25			0.1	0.25	0.3	0.8	C	
Acrylamide		0.03				0.3				0.03			B2	A2
Acronitrile					2		10		1		10			A2
Aldrin		0.25				0.25				0.25			B2	
Ammonia	25	17	35	24			50	35	25	18	35	27		
n-Amyl Acetate	100	532			100	525			100	525				
Antimony and compounds		0.5				0.5				0.5				
Aroclor 1242 and 1254 (PCBs)		0.5				0.5				0.001			B2	
Benzene	10	32			1		5		0.1		1			
Benzoyl peroxide		5				5				5				
Beryllium and compounds		0.002				0.002		0.005		0.0005			B2	A2
1,3-Butadiene	2	4.4			1000	2200								
2-Butanone (MEK)	200	590	300	885	200	590			200	590	300	885	D	
2-Butoxyethanol	25	121			50	240			5	24				
n-Butyl acetate	150	713	200	950	150	710			150	710	200	950		
sec-Butyl acetate	200	950			200	950			200	950				
tert-Butyl acetate	200	950			200	950			200	950				
Butyl mercaptan	0.5	1.8												
Cadmium (as Cd)		0.01				0.005							B1	A2
Carbaryl (Sevin,pesticide)		5				5				5			Not Evaluated	
Carbon disulfide	10	31			20		30		1	3	10	30	Not Evaluated	
Carbon tetrachloride	5	31	10	63	10		25				2	12.6	B2	A3
Chlorobromomethane (Halon 1011)	200	1060			200	1050			200	1050			D	
Chloroform	10	49					5	240			2	9.78	B2	A2

**REGULATORY VALUES**

CHEMICAL	ACGIH TLVs				OSHA PELs				NIOSH RELs				CARCINOGENICITY CLASSIFICATION	
	TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		IRIS	ACGIH
	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m		
Chromic acid and chromates (as CrO <sub>3</sub> )									0.1		0.001			A1
Chromium metal (as Cr)		0.5					1				0.5			A1
Coal tar pitch volatiles		0.2					0.2				0.1		A	A1
Cobalt dust and fume		0.02					0.1				0.05			A3
Copper dust and mist		1					1				1			D
Copper fume		0.2					0.1				0.1			
Cresol	5	22												
Cyanides			4.7	5			5					4.7	5	D
Cyclohexane	300	1030			300	1050			300	1050				
Cyclohexanol	50	206			50	200			50	200				
Cyclohexanone	25	100			50	200			25	100				
Cyclohexane	300	1010			300	1015			300	1015				
Cyclopentadiene	75	203			75	200			75	200				
Dibutyl phosphate	1	8.6	2	17	1	5			1	5	2	10		
Dibutylphthalate		5				5				5			D	
o-Dichlorobenzene	25	150	50	301			50	300			50	300	D	
p-Dichlorobenzene	10	60			75	450							Evaluated	A3
Dichlorodifluoro methane (Freon 12)	1000	4950			1000	4950			1000	4950			Not Evaluated	
Dichloromonofluoro methane (Freon 21, Halon 112)	10	42			1000	4200			10	40				
Dichlorotetrafluoroethane (Freon 114)	1000	6990			1000	7000			1000	7000				
Dichlorvos (pesticide)	0.1	0.9					1				1		B2	
Dieldrin		25					0.25				0.25		B2	
Diethylamine	0.46	2			25	75			10	30	25	75		A4
Dimethylamine	5	9.2	15	27.6	10	18			10	18			Not	
Dimethylformamide	10	30			10	30			10	30			Not	
Dimethylphthalate		5					5				5		D	
Endrin (pesticide)		0.1					0.1				0.1		D	

**REGULATORY VALUES**

CHEMICAL	ACGIH TLVs				OSHA PELs				NIOSH RELs				CARCINOGENICITY CLASSIFICATION	
	TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		IRIS	ACGIH
	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m		
Epichlorohydrin	2	7.6			5	19							B2	A2
2-Ethoxyethanol (Ethylene Glycol monoethyl ether)	5	18			200	740			0.5	1.8			Not Evaluated	
2-Ethoxyethyl acetate (Cellosolve acetate, Ethylene Glycol	5	27			100	540			0.5	2.7				
Ethyl acetate	400	1440			400	1400			400	1400			Not Evaluated	
Ethylamine	5	9.2	15	27.6	10	18			10	18				
Ethylbenzene	100	434	125	543	100	435			100	435	125	545	D	
Ethylenediamine	10	25			10	25			10	25			D	
Ethylene dibromide					20		30		0.045		0.13		B2	A2
Ethylene oxide	1	1.8			1		5		<0.1	<0.18	5	9		A2
Ethyl mercaptan	0.5	1.3					10	25			0.5	1.3		
Fluorides		2.5												
Formaldehyde			0.3	0.37	0.75		2		0.016		0.1		B1	A2
Heptachlor		0.05				0.5				0.5			B2	A3
n-Heptane	400	1640	500	2050	500	2000			85	350	440	1800	D	
n-Hexane	50	176			500	1800			50	180			Not Evaluated	
2-Hexanone (MBK)	5	20			100	410			1	4				
Hexane (MIBK)	50	205	75	307	100	410			50	205	75	300	Not Evaluated	
Hydrazine	0.1	0.13			1	1.3					0.03	0.04	B2	A2
Hydrogen cyanide			4.7	5	10	11					4.7	5	Not Evaluated	
Hydrogen fluoride			3	2.6	3				3	2.5	6	5		
Hydrogen peroxide	1	1.4			1	1.4			1	1.4				
Hydrogen sulfide	10	14	15	21			20				10	15	Not Evaluated	
Hydroquinone		2				2							Not Evaluated	
Isoamyl acetate	100	532			100	525			100	525				
Isobutyl acetate	150	713			150	700			100	700				

## REGULATORY VALUES

CHEMICAL	ACGIH TLVs				OSHA PELs				NIOSH RELs				CARCINOGENICITY CLASSIFICATION	
	TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		IRIS	ACGIH
	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m		
Isobutyl alcohol	50	152			100	300			50	150			Not Evaluated	
Isopropyl acetate	250	1040	310	1290	250	950			250		310			
Isopropyl amine	5	12	10	24	5	12			5		10			
Lindane (pesticide)		0.5				0.5			0.5				Not Evaluated	
Malathion (pesticide)		10				15			10				Not Evaluated	
Methoxychlor (insecticide)		10				15							D	
Methyl acrylate	10	35			10	35			10	35			D	
Methyl cellosolve (EGME)	5	16			25	80			0.1	0.3			Not Evaluated	
Methyl cellosolve acetate	5	24			25	120			0.1	0.5				
Methyl chloride (Monochloro methane)	50	103	100	207	100		200							
Methyl chloroform (1,1,1-Trichloroethane)	350	1910	450	2460	350	1900					350	1900	D	
Methylene Chloride (Dichloroethane)	50	174			500		1000						B2	A2
Methyl methacrylate	100	410			100	410			100	410				
Mineral oil		5		10		5				5		10		
Naphtha (coal tar)					100	400			100	400				
p-Nitroaniline		3			1	6					3			
Nitrobenzene	1	5			1	5			1	5			D	
Paraquat (pesticide)	0.5					0.5				0.1			C	
Parathion (pesticide)		0.1				0.1				0.05			C	
Pentaborane	0.005	0.013	0.015	0.039	0.005	0.01			0.005	0.01	0.015	0.03		
Pentachloronaphthalene (Halowax 1013)		0.5				0.5				0.5				
Pentachlororphenol (fungicide)		0.5				0.5				0.5			B2	
n-Pentane	600	1770	750	2210	1000	2950			120	350	610	1800		
2-Pentanone	200	705	250	881	200	700			150	530				

# REGULATORY VALUES

CHEMICAL	ACGIH TLVs				OSHA PELs				NIOSH RELs				CARCINOGENICITY CLASSIFICATION	
	TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		IRIS	ACGIH
	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m		
Petroleum Distillates (naphtha)	300	1370			500	2000				350		1800		
Phenol	5	19			5	19			5	19	15.6	60	D	
Phenyl ether vapor (Phenoxybenzene)	1	7	2	14	1	7			1	7				
Phenyl Hydrazine	0.1	0.44			5	22					0.14	0.6		
Phosgene	0.1	0.4			0.1	0.4			0.1	0.4	0.2	0.8	Not Evaluated	
Phosgene														
Phosphine (pesticide)	0.3	0.42	1	1.4	0.3	0.4			0.3	0.4	1	1	D	
n-Propyl acetate	200	835	250	1040	200	840			200	840	250	1050		
n-Propyl alcohol	200	492	250	614	200	500			200	500	250	625		
Propylene dichloride (pesticide)	75	347	110	508	75	350							Not Evaluated	
Pyethrum		5				5				5				
Pyridine	5	16			5	15			5	15			Not Evaluated	
Stoddard Solvent (mineral spirits)	100	525			500	2900				350		1800		
Strychnine (pesticide)		0.15				0.15				0.15			Not Evaluated	
Sulfur dioxide	2	5.2	5	13	5	13			2	5	5	13		
Sulfur pentafluoride			0.001	0.1	0.025	0.25					0.01	0.1		
Sulfuryl fluoride	5	21	10	42	5	20			5	20	10	40		
1,1,2,2-Tetrachloro-1,2-difluoroethane (Freon 112)	500	4170			500	4170			500	4170				
1,1,2,2-Tetrachloroethane	1	6.9											C	
Tetrachloroethylene (Perchloroethylene)	25	170	100	685	100		200						Under Review	A3
Tetrahydrofuran	200	590	250	737	200	590			200	590	250	735		
Toluene	50	188			200		300		100	375	150	560	D	
Toluene 2,4-diisocyanate	0.005	0.036	0.02	0.14	0.02	0.14								
o-Toluidine	2	8.8			5	22							A2	
Tributyl phosphate	0.2	2.2			5				0.2	2.5				

**REGULATORY VALUES**

CHEMICAL	ACGIH TLVs				OSHA PELs				NIOSH RELs				CARCINOGENICITY CLASSIFICATION	
	TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		TWA		STEL/CEIL (C)		IRIS	ACGIH
	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m	ppm	mg/cu m		
1,1,2-Trichloroethane	10	55			10	45			10	45			C	
Trichloroethylene	50	269	100	537	100		200						Under Review	A5
1,1,2-Trichloro-1,2,2-trifluoroethane (Freon 113)	1000	7670	1250	9590	1000	7600			1000	7600	1250	9500	Not Evaluated	
Triethylamine	1	4.1	5	20.7	25	100							Not Evaluated	A4
Trifluorobromo methane (Halon 1301)	1000	6090			1000	6100			1000	6100				
Tri orthocresyl phosphate		0.1				0.1					0.1			
Triphenyl phosphate		3				3					3			
Turpentine	100	556			100	560			100	560				
Vinyl chloride	5	13			1		5							A1
Xylenes (o-,m-,p-isomers)	100	434	150	651	100	435			100	435	150	655		
Xyldine (o-,m-,p-, isomers)	0.5	2.5			5	25			2	10				A2

### **III. CARCINOGENICITY DESIGNATION**

#### **EPA**

- A. Human Carcinogen: sufficient evidence from epidemiologic studies to support a causal association between exposure and cancer.
- B. Probable Human Carcinogen: weight of evidence of human carcinogenicity based on epidemiologic studies is limited; agents for which weight of evidence of carcinogenicity based on animals studies is sufficient.
  - B1: Limited evidence of carcinogenicity from epidemiologic studies
  - B2: Sufficient evidence from animal studies; inadequate or no data from epidemiologic studies.
- C. Possible Human Carcinogen: limited evidence of carcinogenicity in animals in the absence of human data.
- D. Not Classifiable as to Human Carcinogenicity: inadequate human and animal evidence of carcinogenicity or no data are available.
- E. Evidence of Non-carcinogenicity for humans: no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies.

#### **ACGIH**

- A1. Confirmed Human Carcinogen: agent is carcinogenic to humans based on epidemiologic studies or, or convincing clinical evidence in, exposed humans.
- A2. Suspected Human Carcinogen: agent is carcinogenic in experimental animals at dose levels, by route(s) of administration, at site(s), of histologic type(s), or by mechanism(s) considered relevant to worker exposure. Available epidemiologic studies are conflicting or insufficient to confirm an increased risk of cancer in exposed humans.
- A3. Animal Carcinogen: agent is carcinogenic in experimental animals at a relatively high dose, by route(s) of administration, at site(s), of histologic types(s), or by mechanism(s) not considered relevant to worker exposure. Available epidemiologic studies do not confirm an increased risk of cancer in exposed humans. Available evidence suggests that the agent is not likely to cause cancer in humans except under uncommon or unlikely routes or levels of exposure.
- A4. Not Classifiable as a Human Carcinogen: inadequate data no which to classify the agent in terms of its carcinogenicity in humans and/or animals.
- A5. Not Suspected as a Human Carcinogen: not suspected to be a human carcinogen on the basis of properly conducted epidemiologic studies in humans. Studies have sufficiently long follow-up, reliable exposure histories, sufficiently high dose, and adequate statistical power to conclude that exposure to the agent does not convey a significant risk of cancer to humans. Evidence suggesting a lack of carcinogenicity in experimental animals will be considered if it is supported by other relevant data.

Substances for which no human or experimental animal carcinogenic data have been reported are assigned no carcinogen designation.

Exposures to carcinogens must be kept to a minimum. Workers exposed to A1 carcinogens without a TLV should be properly equipped to eliminate to the fullest extent possible all exposure to the carcinogen.

### **III. CARCINOGENICITY DESIGNATION**

For A1 carcinogens with a TLV and for A2 and A3 carcinogens, worker exposure by all routes should be carefully controlled to levels as low as reasonably achievable below the TLV.

## **REFERENCES**

Casarett and Doull's Toxicology: The Basic Science of Poisons, 4th Edition. Mary O. Amdur, John Doull, Curtis D. Klaassen, eds., McGraw-Hill, Inc., Health Professions Division, New York, 1991.

HSDB: as a component of TOMES ® (Toxicology, Occupational Medicine & Environmental Series Database), published by MICROMEDEX, INC®, Vol. 26, edition expires Oct. 1995.

IRIS II: an EPA database found as a component of TOMES ® (Toxicology, Occupational Medicine & Environmental Series Database), published by MICROMEDEX, INC®, Vol. 26, edition expires Oct. 1995.

NIOSH Pocket Guide to Hazardous Chemicals, U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, June 1994.